

Rand N. Shulman
Vice President
Health, Safety and Environment
Shell Chemical Company
Shell Oil Products Company

PDCN:88940000329

8EHQ-0395-1308

One Shell Plaza
P.O. Box 2463
Houston TX 77252-2463



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Dear Sir:

SUBJECT: NEUROFUNCTIONAL AND NEUROSTRUCTURAL CHANGES IN THE BRAIN
AND SPINAL CORD OF RATS EXPOSED TO VINYL PIVALATE IN A
10-DAY VAPOR INHALATION TOXICITY STUDY - FINAL REPORT

On June 28, 1994 Shell Oil Company submitted the subject information under TSCA 8(e) (copy attached, no 8EHQ reference number provided). In this original filing, neurofunctional and neurostructural changes were seen in ten male and ten female rats exposed 6 hours/day to 10 daily (5 days/week for 2 weeks) vapor concentrations of 1000 ppm vinyl pivalate (CASRN 3377-92-2) in a repeat exposure vapor inhalation toxicity study. Neurofunctional changes included significant effects on gait, grip strength, and hind leg splay. Neurostructural changes included vacuolation, myelinopathy and axonopathy of the brain and spinal cord.

The study, which was conducted by the Bushy Run Research Center is jointly sponsored by Shell Chemical Company and Union Carbide Chemical and Plastics Co. Since similar findings had been reported previously as a TSCA 8(e) by Union Carbide Corporation for vinyl pivalate dosed orally in acute (8/30/89) and 14-day (5/11/92) toxicity studies in rats, the June 28, 1994 filing by Shell was considered supplemental to that reported in the Union Carbide TSCA 8(e) filings and included a copy of the data tables from the draft, unaudited report. The complete final report is now available and is attached as additional supplemental 8(e) information. The final report does not alter the conclusions contained in the unaudited, draft report.

This final report is filed to provide supplemental information EPA may find useful. In no way is it intended as a waiver of any rights or privileges belonging to Shell Oil Company as the reporting corporation, its agents or employees. The reporting

corporation, its agents and employees, reserve the right to object to this report's use or admissibility in any subsequent judicial or administrative proceeding against the corporation, its agents or employees.

This report has been compiled based on information available as of the date of filing. The corporation, its agents and employees reserve the right to supplement the data contained in this report, and to revise and amend any conclusions drawn therefrom.

This report contains no confidential business information.

The following person should be contacted if you have questions or a need for discussion.

J. C. Willett
Manager, Product Safety and Compliance
Shell Oil Company
P.O. Box 4320
Houston, TX 77210
Telephone No. 713-241-6958
Fax. 713-241-3325

Very truly yours,

A handwritten signature in black ink, appearing to read "R. N. Shulman", with a long horizontal flourish extending to the right.

R. N. Shulman

THG/sjh

Attachments

Shell Oil Company



One Shell Plaza
P.O. Box 4320
Houston, Texas 77210

June 28, 1994

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U.S. Environmental Protection Agency
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AND SPINAL CORD OF RATS EXPOSED TO VINYL PIVALATE IN A
10-DAY VAPOR INHALATION TOXICITY STUDY

The following information is submitted under TSCA 8(e).

Neurofunctional and neurostructural changes were seen in ten male and ten female rats exposed 6 hours/day to 10 daily (5 days/week for 2 weeks) vapor concentrations of 1000 ppm vinyl pivalate (CASRN 3377-92-2) in a repeat exposure vapor inhalation toxicity study. Neurofunctional changes included significant effects on gait, grip strength, and hind leg splay. Neurostructural changes included vacuolation, myelinopathy and axonopathy of the brain and spinal cord.

The study, which was conducted by the Bushy Run Research Center is jointly sponsored by Shell Chemical Company and Union Carbide Chemical and Plastics Company. It is Shell's understanding that similar findings have been reported previously as a TSCA 8(e) by Union Carbide Corporation for vinyl pivalate dosed orally in acute (8/30/89) and 14-day (5/11/92) toxicity studies in rats. Thus, this information may be considered supplemental to that reported in the Union Carbide TSCA 8(e) filings.

Attached is a copy of the data tables from the draft, unaudited report, which presents the functional observation battery and microscopy results. The complete final report will be sent to the Agency when available.

This report is filed to provide information EPA may find useful. In no way is it intended as a waiver of any rights or privileges belonging to Shell Oil Company as the reporting corporation, its agents or employees. The reporting corporation, its agents and

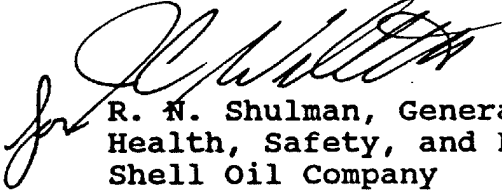
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J. C. Willett
Manager, Product Safety and Compliance
Shell Oil Company
P.O. Box 4320
Houston, TX 77210
Telephone No. 713-241-6958
Fax. 713-241-3325

Very truly yours,



R. N. Shulman, General Manager
Health, Safety, and Environment
Shell Oil Company

THG/sjh

Attachments



BUSHY RUN RESEARCH CENTER

6702 Mellon Road, Export, Pennsylvania 15632-8902

Telephone (412) 733-5200
Telecopier (412) 733-4804

STUDY TITLE

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

TEST SUBSTANCE

Vinyl Pivalate

DATA REQUIREMENT

Not Applicable

AUTHORS

J. C. Norris, J. S. Chun, and W. J. Kintigh

STUDY COMPLETION DATE

February 10, 1995

PERFORMING LABORATORY

Bushy Run Research Center (BRRC)
Union Carbide Corporation (UCC)
6702 Mellon Road
Export, PA 15632-8902

LABORATORY PROJECT ID

94U1377

SPONSORS

UCAR Emulsion Systems
Union Carbide Corporation (UCC)
410 Gregson Drive
Cary, NC 27511

Shell Oil Company
One Shell Plaza
P. O. Box 4320
Houston, TX 77210

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

CONFIDENTIALITY STATEMENT

This report is Union Carbide Corporation and Shell Oil Company Business Confidential and is not to be released outside of either Corporation/Company without the written consent of the Sponsors.

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

COMPLIANCE WITH GOOD LABORATORY PRACTICE STANDARDS

The portions of this study conducted by BRRC meet the requirements of the following Good Laboratory Practice Standards: Toxic Substances Control Act (TSCA), 40 CFR Part 792; Organisation for Economic Co-operation and Development (OECD), C(81)30(Final) with exceptions. These exceptions are:

1. The test substance was not analyzed prior to exposures.
2. The test substance was returned to the Sponsor prior to the Study Completion Date.
3. Calibration records for the MSA® Oxygen Indicator Model 245R cannot be located.

Study Director:


James C. Norris, Ph.D.

 2/10/95
Date

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Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats**SUMMARY**

Four groups, each containing 10 Fischer 344 rats/sex, were exposed to either filtered air (control) or vinyl pivalate vapor (CAS No. 3377-92-2) at target concentrations of 0 (control), 100, 500, or 1000 ppm. Animals were exposed for 6 hr/day for 5 consecutive days during the first week. During the second week, male and female rats designated for neuroanatomic evaluation were exposed for 6 hr/day for 3 and 4 days, respectively. All remaining animals (5 rats/sex/group) were exposed for 5 consecutive days during the second week. Monitors for toxic effects included detailed clinical observations, body and organ weights, food consumption, functional observations, hematologic evaluations, necropsy observations, and microscopic evaluations.

Mean vinyl pivalate concentrations of 103 (\pm 1.3), 497 (\pm 6.5), and 993 (\pm 18.3) ppm were measured. No mortality occurred during the study. Clinical signs were observed for both sexes of rats during exposures to 500 and 1000 ppm and included hypoactivity, lack of a startle reflex, and blepharospasm. Deep breathing was also noted in rats from the 1000 ppm group during the exposures. The primary clinical sign observed following the exposures was incoordination which was noted in all male and female rats from the 1000 ppm group. Two of these females were also noted to be hypoactive on Day 11. Other exposure-related clinical signs observed in males and females from the 1000 ppm group included an increased incidence of swollen periocular tissue, periocular encrustation, and perinasal encrustation (females only). The incidence of periocular encrustation was also slightly increased in males from the 500 ppm group. Absolute body weight and/or body weight gain were decreased in males from the 1000 ppm group and females from the 500 and 1000 ppm groups. Food consumption was decreased in males and females from the 500 and 1000 ppm groups. Decreases in erythrocyte count, hemoglobin, and hematocrit were observed in males from the 500 and 1000 ppm groups and females from all vinyl pivalate-exposed groups. Mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) were also decreased in males and females from the 1000 ppm group. Concentration-related increases in liver weight (absolute and relative to body and brain weights) were observed for females. An increase in absolute and relative (as a percentage of body and brain weights) liver weight was also noted for male rats from the 1000 ppm group. There were no histopathological lesions in the liver that were considered to be exposure related. A decreased absolute brain weight was noted for females from the 1000 ppm group. Mean absolute and both relative kidney weights tended to be slightly increased in males from the 1000 ppm group and females from all vinyl pivalate-exposed groups. There were no exposure-related microscopic lesions observed in the kidneys, and the biological significance of this finding is not clear.

The Functional Observational Battery (FOB) provided evidence of neurobehavioral alterations in the animals from the 1000 ppm group, and the findings included abnormal or uncoordinated gait, decreased rearing (males only), decreased forelimb grip strength, and increased landing hind leg splay.

The only gross lesions which may be related to the exposure were periocular and/or perinasal crust/scab/scale and periocular swelling in the 500 and 1000 ppm groups.

Upon microscopic evaluation, various lesions which were attributed to exposure to vinyl pivalate were observed in the brain and spinal cords of all rats from the 1000 ppm group (both perfused and nonperfused). In nonperfused rats, the lesions consisted of vacuolation and spongiosis in the brain stem (medulla and pons) and the ventral/lateral funiculi (white matter tracts) of the spinal cord. In perfused rats, the lesions were similar in location and nature to those seen in the nonperfused animals. The lesions included myelinopathy and axonopathy observed consistently in the white matter of the pons and medulla oblongata, in the vestibular nuclei, midbrain, and trigeminal tracts, and in the ventral and lateral funiculi of the spinal cord.

Exposure of rats to 500 and 1000 ppm of vinyl pivalate vapor produced various clinical signs, hematologic changes suggestive of mild anemia, and effects on body weight, food consumption, and organ weights. Evidence of neurobehavioral alterations and microscopic lesions in the brain and spinal cord were noted in animals exposed to 1000 ppm. Hematologic and organ weight changes were observed in females even at the lowest concentration (100 ppm). Thus, the no-observed-effect level (NOEL) of vinyl pivalate for males was considered to be 100 ppm under the conditions of this study. For females, the no-observed-adverse-effect level (NOAEL) was considered to be 100 ppm.

OBJECTIVE

The objective of this study was to determine and evaluate the toxic effects in rats which may occur from short-term repeated inhalation exposure to vinyl pivalate vapor.

BACKGROUND INFORMATION

Several acute studies were conducted with vinyl pivalate at Bushy Run Research Center (BRRC Report 52-110). Vinyl pivalate was considered to be moderately toxic when administered perorally; the LD50 for the male rat was 3.73 ml/kg and for the female rat was 2.14 ml/kg. When administered percutaneously, vinyl pivalate was considered to be moderately toxic; the LD50 for the male rabbit was 8.57 ml/kg and for the female rabbit was 13.5 ml/kg. When rats were exposed to substantially saturated vapor (static), the LT50 was 17.3 minutes. Transient, but moderate erythema and edema were observed on 1 of 6 rabbits that were occluded for 4 hours following the application of 0.5 ml of vinyl pivalate. The irritation subsided after 1 day. No corneal injury or iritis was observed in any of 6 eyes after treatment with 0.1 ml. Minor conjunctival irritation did occur in 3 of 6 eyes, but all eyes were healed after 24 hours.

A single exposure oral neurotoxicity study was also conducted at BRRC (BRRC Report 52-133). In this study, male rats were treated on one occasion with undiluted vinyl pivalate at dosage levels of 0.0 (10 animals), 2.0 (7 animals), or 3.0 ml/kg of body weight (5 animals). All 5 animals in the 3.0 ml/kg group died or were sacrificed in a moribund condition 1 day after treatment. Two animals in the 2.0 ml/kg group were sacrificed 3 days after treatment and the remaining animals were sacrificed 15 days after treatment. Functional Observational Battery (FOB) evaluations were performed on the 2.0 ml/kg group of animals 1 day after treatment and 14 days after treatment. Treatment with 2.0 ml/kg caused sluggishness (transient) and hind limb gait impairments. Behavior alterations, observed 1 and 14 days after treatment, were consistent with the clinical signs of toxicity and included mild gait alterations, alterations in hind limb grip strength and landing foot splay, and hypoactivity (1 day after treatment only). Microscopic lesions observed following treatment with 2.0 ml/kg included minimal to marked myelin sheath swelling and degeneration within the central nervous system. Based on a comparison with lesions resulting from a single peroral dose of 4.0 ml/kg (BRRC Report 52-110), the severity of the lesions observed increased with increasing dose. Lesions tended to be more severe 14 days after treatment than 3 days after treatment. Under the conditions of this study, a single peroral treatment of male rats with a maximum nonlethal dose of vinyl pivalate (2.0 ml/kg) produced mild to moderate behavioral changes and moderate pathologic alterations in the central nervous system.

Vinyl pivalate was also tested for potential mutagenic activity using the Salmonella/microsome bacterial mutagenicity (Ames) assay (BRRC Report 52-146) and was not considered to be mutagenic under the conditions of this study.

A study to measure the rates of hydrolysis of various vinyl ester compounds in rat liver homogenates was conducted at BRRC (BRRC Report 92U1149). The disappearance of vinyl pivalate and other vinyl ester compounds in Fischer 344 male rat liver homogenates was measured. The auto-hydrolysis of selected

compounds was also evaluated at pH 2, and an evaluation was made of the effect of heat treatment on enzymatic hydrolysis. The nonenzymatic degradation rate of vinyl pivalate at pH 2 was found to be 2 to 3 orders of magnitude slower than the metabolic degradation rates measured using rat liver homogenates. Furthermore, heat-inactivation (70°C/20 min) of liver homogenates inhibited hydrolysis. The nonenzymatic degradation rate would, therefore, not be expected to substantially influence the overall breakdown of vinyl pivalate in vivo when compared to the enzymatic rates of degradation.

An additional investigation was conducted with male Fischer 344 rats to evaluate the potential for reactive intermediates to be produced during the metabolism of a number of vinyl esters (BRRC Report 92U1190). The decrease in the in vivo levels of rat liver reduced glutathione (GSH) was considered an indication of the production of reactive intermediates. While a 0.8 ml/kg dose of vinyl acetate killed 3 of 6 rats within 5 minutes after intraperitoneal dosing, the results from the investigation indicated that the metabolism of the compound resulted in the production of biochemically reactive intermediates that may be conjugated by GSH.

Fischer 344 rats (6/sex/group) were administered vinyl pivalate in corn oil by gavage at dosages of 50, 200, 1000, or 2000 mg/kg/day (BRRC 93U1317). All animals in the 2000 mg/kg/day dose group died prior to receiving the fourth daily dose. No additional mortality was observed. There were no effects on mean food consumption, mean body weight or body weight gain throughout the study that were considered to be treatment-related. Treatment-related clinical signs of toxicity were limited to animals from the 2000 mg/kg/day dose group shortly after dosing and included primarily salivation/perioral wetness, hypoactivity and/or incoordination. Prior to death on Study Day 3, several animals from this dose group had urine stains, labored respiration and/or perinasal encrustation and were hypoactive, incoordinated and/or prostrate. Necropsy observations of these animals indicated a color change of the stomach in most animals. Microscopic findings were primarily associated with the nonglandular stomachs of these animals and included hemorrhage, edema, gastritis and hyperkeratosis (1 animal) and serositis (1 animal). A neurological functional observational battery (FOB) was conducted on Study Days 12, 13, and 14 and findings observed on Day 12 included an abnormal gait, decreased number of times the animal reared onto its hind legs during the 2 minute observation period, and increased landing hind leg splay in both male and female animals. Female rats also had decreased grip strength and a slight decrease in mean body temperature. The FOB conducted over the next two days generally indicated a recovery from the functional effects. Histopathological evaluation of the nervous system in both perfused (male only) and nonperfused (male and female) animals from the 1000 mg/kg/day dose group indicated vacuolation and/or spongiosis of the white matter primarily of the brain stem, including the medulla oblongata and pons (1 perfused male animal had lesions in the midbrain). When the spinal cord from animals in this dose group was examined (perfused males only), similar lesions were also observed. There were no lesions observed in the peripheral nervous system of any animals. There were no treatment-related lesions observed in any animal from any other dose group. Treatment with vinyl pivalate at 1000 mg/kg/day resulted in hematology changes suggestive of mild anemia and increases in liver (also in the 200 mg/kg/day dose group), spleen and kidney weights. No histopathological findings were observed in the liver, kidney, and spleen.

The no-observed-adverse-effect level of vinyl pivalate under the conditions of this study was considered to be 200 mg/kg/day.

TARGET CONCENTRATION SELECTION

Target vinyl pivalate vapor concentrations of 0 (control), 100, 500, or 1000 ppm were selected by the Sponsor based on the results from the acute studies.

MATERIALS AND METHODS

The protocol and any protocol amendments detailing the design and conduct of this study are included in Appendix 10. Protocol deviations are also included in Appendix 10.

Test Substance

One 5-gallon container of vinyl pivalate (VYNATE® Neo-5 Monomer, Lot No. JGT-3B, CAS No. 3377-92-2) was received on February 15, 1994, from Union Carbide Corporation (South Charleston, WV) and assigned BRRRC Sample No. 57-036. The test substance was a clear, colorless liquid. The test substance was stored at room temperature. The purity of the test substance was determined by the GLP Analytical Skill Center at the UCC South Charleston, WV, Technical Center to be 99.95%, and the report is included in Appendix 1.

Animals and Husbandry

Fifty-eight male and 55 female Fischer 344 rats arrived on February 15, 1994, from Harlan Sprague Dawley, Inc., Indianapolis, IN. They were designated by the supplier to be approximately 42 days old (the birth date was recorded as January 4, 1994) upon arrival. The females were nulliparous and nonpregnant.

Animals were housed in Room 102 from arrival to termination of the study, except during exposures. Within 3 days of receipt, the animals were examined by a clinical veterinarian and a pretest health screen for representative animals was initiated. The health screen included full necropsy, histologic examination of selected tissues, including respiratory tract, and examinations for fecal parasites. Approximately 1 week later, blood samples were collected for serum viral antibody analyses. Based on the results of these data, the clinical veterinarian indicated that these animals were in good health and suitable for use.

All animals were assigned unique numbers and identified by cage tags. Animals considered available for the study were also identified by a tail tattooing procedure. Animals selected for the pretest health screen were identified by a toe-clipping procedure after sacrifice.

The animals were housed 2/cage for approximately 9 days, then individually housed for the duration of the study. The animals were housed in stainless steel, wire mesh cages (22.5 x 15.5 x 18.0 cm), except during exposures and functional observational battery (FOB) testing. The purpose of the double housing was to help acclimate the animals to their new surroundings. DACB® (Deotized Animal Cage Board; Shepherd Specialty Papers, Inc.) was placed under each stainless steel cage and changed regularly. Cages were changed and sanitized at least once every 2 weeks. The animals were housed in

polycarbonate cages (26.7 x 24.1 x 20.3 cm) for FOB testing. ALPHA-dri® (Shepherd Specialty Papers, Inc.) bedding was placed in the polycarbonate cages. An automatic timer was set to provide fluorescent lighting for a 12-hour photoperiod (approximately 0500 to 1700 hours for the light phase). Temperature and relative humidity were recorded (Cole-Parmer Hygrothermograph® Seven-Day Continuous Recorder, Model No. 8368-00, Cole-Parmer Instrument Co., Chicago, IL). Temperature was routinely maintained at 66-77°F; relative humidity was routinely maintained at 40-70%.

Tap water (Municipal Authority of Westmoreland County, Greensburg, PA) was available ad libitum except during exposures and was delivered by an automatic watering system with demand control valves mounted on each rack. Water analyses were provided by the supplier, and Chester Lab and RJ Lee Group, Inc. at regular intervals. EPA standards for maximum levels of contaminants were not exceeded. Ground Lab Diet™ The Richmond Standard™ Certified Rodent Diet #5002 (PMI Feeds, Inc.) was available ad libitum except during exposures. Analyses for chemical composition and possible contaminants of each feed lot were performed by PMI Feeds, Inc., and the results were included in the raw data.

Animal Acclimation

The acclimation period was approximately 2 weeks. During this period, the animals were weighed at least 2 times at scheduled intervals. Detailed clinical observations were conducted in conjunction with body weight measurements. Cage-side animal observations were conducted at least once daily, and mortality checks were conducted twice daily (morning and afternoon). The animals were examined just prior to the end of the acclimation period by a clinical veterinarian. Animals considered unacceptable for the study, based on the clinical signs, body weight, or body weight gain, were rejected. The fate of rejected animals and the reasons for rejection were documented in the raw data.

Study Organization

Following the second pretest body weight, the animals were assigned to 3 exposure groups and a control group using a stratified randomization procedure based on body weight. At the time of group assignment, only animals with body weight within $\pm 20\%$ of the population mean for each sex were included. The body weight range on the day of first exposure was 144.2 to 183.7 g for males and 112.9 to 139.3 g for females. The following table summarizes the organization of the study.

Group	Number of Animals		Target Concentration (ppm)
	Male	Female	
Control	10	10	0
Low	10	10	100
Intermediate	10	10	500
High	10	10	1000

The exposures began on February 28, 1994 (Study Day 1). Animals were exposed for 6 hours/day for 5 consecutive days during the first week. The 6-hour exposure period was defined as the time when the generation system was turned on and subsequently turned off. After 2 days without exposure, the animals were exposed for 3 (males designated for neuroanatomic evaluation), 4 (females designated for neuroanatomic evaluation) or 5 consecutive days during the second week. All control animals were exposed to filtered air only using the same exposure regimen. Five males and 5 females from each group designated for neuroanatomic pathology evaluation were sacrificed on March 10 and 11, respectively. All remaining animals were sacrificed on March 12, 1994, after 10 exposures.

Exposure to Test Substance

Inhalation Chamber Description and Operation

The inhalation chambers (Wahmann Manufacturing Company, Timonium, MD) used for this study were located in Room 137. The chambers, constructed from stainless steel with glass windows for animal observation, were rectangular (101 x 101 x 60.2 cm) in shape with a pyramidal top and bottom. The volume of each chamber was approximately 900 l, and the airflow was approximately 200 l/min (13 air changes/hour). A Dwyer Magnehelic® pressure gauge (Dwyer Instruments, Inc., Michigan City, IN) was used to monitor chamber airflow. The theoretically-derived time (t_{99}) required for each chamber to reach 99% of the target concentration was calculated to be approximately 21 minutes.

Chamber temperature and relative humidity were recorded using a Fisherbrand® dial type thermometer (Fisher Scientific, Pittsburgh, PA) and an Airguide humidity indicator (Airguide Instrument Co., Chicago, IL), respectively. Temperature and relative humidity measurements were recorded approximately 2 times during each hour of exposure.

Vapor Generation

Liquid vinyl pivalate was metered from a piston pump (RP-G6-0, 1/8-inch piston FMI fluid pump for the 100 ppm exposure chamber; RP-G20-0, 1/8-inch piston FMI fluid pump for the 500 ppm exposure chamber; and RP-G6-2, 3/8-inch piston FMI fluid pump for the 1000 ppm exposure chamber; Fluid Metering, Inc., Oyster Bay, NY) into a heated glass evaporator similar in design to that described by Snellings and Dodd (1990). The design of the glass evaporator was a cylindrical column with spiral ridges inside the column. A coiled heating wire was placed on the outside of the column under the ridges to aid in the evaporation of the liquid test substance. The temperature in the evaporator was maintained at the level sufficient to vaporize the test substance. Evaporator temperatures were determined without the test substance during preliminary level setting and on Exposure Day 6 following the 6-hour exposure period using a thermocouple attached to a digital recorder (Type K thermocouple with a Fluke 51 K/J Thermometer, John Fluke Mfg. Co., Inc., Everett, WA). The temperature probe was positioned on the glass evaporator at the first spiral from the top. The oxygen content of the exposure chambers was also measured during preliminary level setting and on Study Day 6 using an MSA® Oxygen Indicator Model 245R (Mine Safety Appliances, Pittsburgh, PA).

Chamber Atmosphere Measurements

Chamber concentrations of vinyl pivalate vapor were analyzed approximately twice each hour during each 6-hour exposure by flame ionization gas chromatography. A complete description of the analytical procedures is included in Appendix 1.

Observations and Measurements

In-life Evaluations

All animals were individually observed for signs of toxic effects except during the exposures. During the exposures, observations were recorded on a group basis. Preceding each exposure, detailed observations were performed on all animals. Following each exposure, observations were recorded for animals exhibiting overt clinical signs. On nonexposure days, the animals were observed once a day for detailed examinations for clinical signs and twice a day for mortality.

Body weight data were collected for all animals on the morning prior to initiation of the first exposure (denoted as Study Day 1 in the tables), and on Study Days 2, 5, 8, and 9 for all animals. In addition, body weights were measured at Day 12 and immediately preceding sacrifice for all animals (excluding animals designated for the neuroanatomic pathology evaluations).

Food consumption was measured for all animals for intervals, Day 1-5, 5-8, and 8-10.

Neurobehavioral Evaluations

The behavioral function of all animals was evaluated using a screening battery of tests (FOB) designed to detect gross alterations in nervous system function. FOB evaluations were performed during the week prior to the exposure, and on the morning prior to the eighth (males) or ninth (females) exposure. The animals were observed by trained technicians who were unaware of the animals' exposure group. Two different observers were used to evaluate each sex. Each observer evaluated the same animals from that one sex at each testing period.

The endpoints included in the FOB are listed below. An overview of the FOB and the scoring criteria employed are included in Appendix 7.

cage posture	handling reactivity	involuntary muscular movements
vocalization	palpebral closure	unusual behavior
gait	body position	breathing pattern
arousal	defecation	urination
rears	approach response	startle response
tail pinch response	pupil size	muscle tone
piloerection	lacrimation	salivation
fur appearance	crusts	additional observations
visual placing	grip strength	core body temperature
body weight	air righting	hind leg splay
ataxia		

Clinical Pathology Evaluations

Blood samples for all clinical pathology analyses were collected by retroorbital bleeding from methoxyflurane anesthetized rats following the eighth exposure for males and following the ninth exposure for females. Rats were not fasted prior to bleeding. All analyses were performed in a predetermined alternating (1 animal from each group, then repeating) order.

The following parameters were measured or calculated:

Hematology

hematocrit	total leukocyte count
hemoglobin	differential leukocyte count
erythrocyte count	platelet count
mean corpuscular volume (MCV)	
mean corpuscular hemoglobin (MCH)	
mean corpuscular hemoglobin concentration (MCHC)	

Details of the clinical pathology procedures are included in Appendix 3.

Anatomic Pathology Evaluations (Nonperfused Rats)

At the end of exposure (Study Day 13), animals (5 rats/sex/group) were anesthetized with halothane and euthanized by severing their brachial vessels to permit exsanguination. On the day of sacrifice, body weight was obtained to allow expression of relative organ weights. A complete necropsy which included examination of the thoracic cavity was performed on all animals. The liver, kidneys, lungs, brain (including brain stem), spleen, heart, adrenals, testes (males), and ovaries (females) were weighed for all sacrificed animals. The following tissues were collected and retained in 10% neutral buffered formalin:

<u>gross lesions</u>	ileum
<u>lungs</u> (with mainstem bronchi)	cecum
<u>nasopharyngeal tissue</u>	colon
<u>brain</u>	rectum
cerebral cortex	mammary gland (females)
cerebellar cortex	skeletal muscle
medulla/pons	(gastrocnemius)
pituitary	sternum
thyroid-parathyroid complex	femur (including articular surface)
thymic region	<u>trachea</u>
sternum	<u>heart</u>
salivary gland	<u>liver</u>
pancreas	<u>spleen</u>
epididymis	<u>kidneys</u>
prostate	<u>adrenals</u>
seminal vesicles	<u>testes</u>
vagina	ovaries

uterus (corpus and
cervix)
aorta
skin
esophagus
stomach
duodenum
jejunum

urinary bladder
sciatic nerve
lymph node, submandibular
eyes
spinal cord
larynx
bone marrow smear

Tails were saved for identification purposes.

The underlined tissues from all nonperfused animals from the control and high concentration groups from the Day 13 sacrifice were processed histologically and examined microscopically. In addition, the brain and spinal cord for those animals from the low and intermediate dose groups were examined.

Neuroanatomic Pathology Evaluations (Perfused Rats)

Five rats/sex/group designated for neuropathology evaluations were anesthetized with an i.p. injection of a mixture of sodium pentobarbital and heparin following the eighth exposure for males and ninth exposure for females. The following tissues were removed and immersion fixed in a refrigerated solution of 5% glutaraldehyde:

brain	dorsal root ganglia
cerebral cortex	dorsal and ventral nerve roots
midbrain	Gasserian ganglia
cerebellar cortex	sciatic nerve
medulla/pons	nerve, tibial
spinal cord	nerve, sural
	nerve, peroneal

Tails were saved for identification purposes.

Tissues examined by light microscopy were stored, after trimming, in 10% neutral buffered formalin (NBF), and those tissues retained for a possible electron microscopic evaluation were stored refrigerated in a solution of 5% glutaraldehyde. Microscopic examinations were performed on the above tissues for 5 animals/sex from the control and high exposure groups. In addition, brain and spinal cord were examined for low and intermediate exposure groups. The tissues to be examined were embedded in paraffin and stained with hematoxylin and eosin, luxol fast blue and the Bielschowsky's technique. The peripheral nerves were embedded in glycol methacrylate and stained with hematoxylin and eosin, toluidine blue, and the Bielschowsky's technique.

Additional details of the anatomic pathology procedures are included in Appendix 2.

Data Analyses

The data for quantitative continuous variables were intercompared for the 3 exposure groups and the control group by use of Levene's test for equality of variances, analysis of variance (ANOVA), and t-tests. The t-tests were used

when the F value from the ANOVA was significant. When Levene's test indicated similar variances, and the ANOVA was significant, a pooled t-test was used for pairwise comparisons. When Levene's test indicated heterogeneous variances, all groups were compared by an ANOVA for unequal variances followed, when necessary, by a separate variance t-test for pairwise comparisons.

Incidence data were compared using the appropriate statistical test, generally Fisher's Exact Test. Incidence data for select FOB endpoints with ordered severity scores were analyzed for group differences using Gamma, Kendall's Tau-B, Stuart's Tau-C, and Somers' D measures of association.

For all statistical tests, the probability value of < 0.05 (two-tailed) was used as the critical level of significance.

Various models of calculators, computers, and computer programs may have been used to analyze data for this study. Since various models round or truncate numbers differently, values in some tables may differ slightly from those in other tables or from independently calculated data. The integrity of the study and interpretation of the data were unaffected by these differences.

RETENTION OF RECORDS

All raw data, documentation, the protocol and any amendments, specimens, and a copy of the final report generated as a result of this study will be retained in the BRRC/UCC Archives in Morrisville, VT and Wampum, PA (wet Tissues) for at least 10 years. A reserve sample of the test substance was not retained at BRRC due to the possibility of hazardous polymerization.

RESULTS AND DISCUSSION

All references of differences in group mean values in the following text refer to comparisons of statistically significant differences between the exposure group and the control group, unless otherwise noted. Repeated reference to the control and the statistical significance will not be made in order to simplify the text.

Chamber Atmosphere

Detailed results and discussion of the chamber atmosphere measurements are included in Appendix 1.

Gas chromatographic analyses of the chamber atmosphere resulted in mean (\pm SD) concentrations of 103 (\pm 1.3), 497 (\pm 6.5), and 993 (\pm 18.3) ppm for the target concentrations of 100, 500, and 1000 ppm, respectively. The means of daily mean analytical-to-nominal concentration ratios were 0.94, 0.93, and 0.94, for vinyl pivalate target concentrations of 100, 500, and 1000 ppm, respectively. The means of the daily mean temperature values were 22, 23, 22, and 21°C, and the means of the daily mean relative humidity values were 54, 53, 45, and 47% for the 0, 100, 500, and 1000 ppm exposure concentrations, respectively.

Clinical Observations

Summaries of the clinical observations are presented in Tables 1 and 2. The clinical signs observed during exposures are located in the raw data. Individual animal clinical observation data are included in Appendix 4.

No mortality occurred during the study. Clinical signs noted in rats during exposures to 500 and 1000 ppm included hypoactivity, lack of startle reflex, and blepharospasm. Deep breathing was also noted on Day 3 in rats from the 1000 ppm group. No exposure-related clinical signs were noted for animals during exposures to 100 ppm of vinyl pivalate vapor.

The primary clinical sign observed following the exposures considered to be exposure related was incoordination which was noted in all male and female rats from the 1000 ppm group. Two of these females were considered to be hypoactive on Day 11. Other exposure-related clinical signs observed in males and females from the 1000 ppm group were increased incidence of swollen periocular tissue, periocular encrustation, and perinasal encrustation (females only). The incidence of periocular encrustation was also slightly increased in males from the 500 ppm group. No exposure-related clinical signs were observed in animals from the 100 ppm group.

Body Weights

Summaries of absolute body weight and body weight gain are presented in Tables 3 to 6. Individual animal body weight data are included in Appendix 5.

Absolute body weight was decreased after Day 2 for males and females from the 1000 ppm group although the difference was not statistically significant in males. Just prior to sacrifice of animals assigned to the perfused group on Days 11 (males) and 12 (females), the body weight decrease was 6 and 7% for males and females, respectively, when compared to the controls. Mean body weight gain was decreased for males from the 100 ppm group on Day 1 to 2, from the 500 ppm group on Days 1 to 2, 8 to 9 (nonstatistically significant), and 9 to 12 (nonstatistically significant). From the 1000 ppm group for the males, the mean body weight gains were decreased on Days 2 to 5 and 9 to 12 and were decreased nonstatistically significantly on Days 1 to 2, 5 to 8, and 8 to 9. Mean body weight gain was decreased for females from the 500 ppm group on Days 1 to 2, 5 to 8 (nonstatistically significant), 8 to 9 (nonstatistically significant), and from the 1000 ppm group on Days 2 to 5, 5 to 8 (nonstatistically significant), and 8 to 9 (nonstatistically significant). Mean body weight gain was increased for females from the 500 ppm group on Days 9 to 12 (nonstatistically significant).

The slight, but statistically significant, decreases in body weight gain observed for males from the 100 and 500 ppm groups on Day 1 to 2 may have been related to the stress rather than a direct exposure-related effect, since decreases of this magnitude were not noted in the 1000 ppm group.

Food Consumption

Summaries of food consumption data are presented in Tables 7 and 8. Individual animal food consumption data are included in Appendix 6.

Food consumption was decreased for the males in the 500 ppm group on Day 8 to 10 by 8.2%, and in the 1000 ppm group on Day 1 to 5 by 29% and on Day 8 to 10 by 24%. For the females food consumption was decreased in the 500 ppm group on Day 1 to 5 by 9% and on Day 8 to 10 by 7%, and in the 1000 ppm on Day 1 to 5 by 16% and on Day 8 to 10 by 20.2%. No exposure-related changes in food consumption were observed in males and females from the 100 ppm group for any measurement periods and in animals from all exposure groups during the nonexposure period (Day 5 to 8 measurement period). A slight increase in food consumption observed in females from the 100 ppm group was not considered to be exposure related due to the lack of a concentration-response relationship.

Functional Observations

Summaries of the functional observations are presented in Tables 11 to 14. Individual animal data are included in Appendix 7. Figure 1 represents exposure-response curves for selected FOB parameters at each test session.

Functional alterations were obvious in both male and female rats during the FOB evaluation conducted in the morning following the seventh (males) and eighth (females) exposure to 1000 ppm of vinyl pivalate vapor. Uncoordinated or abnormal gait was observed in almost all animals in the 1000 ppm group while normal gait was observed in all control animals. The number of times the animal reared onto its hind legs during the 2-minute observation period was decreased (approximately 22%) in males, although it was not statistically significant. Mean forelimb grip strength measurement was decreased for both male and female rats. The decrease was approximately 25%. Landing hind leg spray was increased for both male and female rats and the value was approximately double the value of the controls.

Clinical Pathology Evaluations

Summaries of the hematology measurements are presented in Tables 9 and 10. Individual clinical pathology data are included in Appendix 9. Detailed results and discussion of the clinical pathology measurements are included in Appendix 3.

Decreases in mean erythrocyte count, hemoglobin, and hematocrit were observed in males from the 500 and 1000 ppm groups and females from all vinyl pivalate-exposed groups. MCH and MCHC were also decreased in males and females from the 1000 ppm group. All other various changes noted upon hematologic evaluations were not considered to be exposure related or biologically significant since the changes were small, inconsistent, and/or the control values were greater than the normal ranges for this strain and age of rats.

Organ Weights, Necropsy Observations, and Microscopic Diagnoses

Summary results of organ weights, organ weights relative to final body weight, and organ weights relative to brain weight are presented in Tables 15 to 20. Summary results of nonperfused necropsy observations are presented in Tables 21 and 22. Summary results of perfused necropsy observations are presented in Tables 23 and 24. Summary results of nonperfused microscopic diagnoses by grade are presented in Tables 25 and 26. The tissue abbreviations used for the neuropathology evaluation is presented in Table 27. Summary results of perfused microscopic diagnoses by grade are presented in Tables 28 to 29.

Individual anatomic pathology data are included in Appendix 8. Detailed results and discussion of the anatomic pathology results are included in Appendix 2.

Mean absolute and relative liver weights were increased in males from the 1000 ppm group and females from the 500 and 1000 ppm groups. The increases were approximately 20-30% for animals from the 1000 ppm group and 15% for females from the 500 ppm group. Mean absolute and relative liver weights tended to be slightly increased (less than 10%) in females from the 100 ppm group, although only statistically significant for liver weight relative to the final body weight. There were no histopathological lesions in the liver that were considered to be exposure related.

Mean relative (as a percentage of body weight) kidney weights were increased in males from the 500 and 1000 ppm groups. Mean absolute and relative (as a percentage of brain weight) kidney weights were also slightly increased in males from the 1000 ppm group although the difference was not statistically significant. Mean absolute and relative kidney weights for females from all vinyl pivalate-exposed groups were increased, except the absolute weights were not statistically significant. There were no exposure-related microscopic lesions observed in the kidneys, and the biological significance of this finding is not clear.

The only other organ weight change which may be related to the exposure was a decreased absolute brain weight in females from the 1000 ppm group. The increased heart weight relative to final body weight observed in males from the 1000 ppm group was due to the decreased body weight and was not considered to be exposure related.

The only gross lesions which may be related to the exposure were periocular and/or perinasal crust/scab/scale and periocular swelling. These lesions were observed in all exposure groups including controls; however, the incidence was slightly higher in the 500 and 1000 ppm groups than in the controls. This increase may be due to the irritating effects of vinyl pivalate.

Various microscopic lesions which were attributed to exposure to vinyl pivalate were observed in the brain and spinal cords of all rats, both perfused and nonperfused, from the 1000 ppm group. In nonperfused rats, the lesions consisted of vacuolation and spongiosis in the brain stem (medulla and pons) and the ventral/lateral funiculi (white matter tracts) of the spinal cord. In perfused rats, the lesions were similar in location and nature to those seen in the nonperfused animals. The lesions included myelinopathy and axonopathy observed consistently in the white matter of the pons and medulla oblongata, in the vestibular nuclei, midbrain, and trigeminal tracts, and in the ventral and lateral funiculi of the spinal cord. There were no similar lesions in rats from the 100 and 500 ppm groups. Other than the nervous system, there were no exposure-related lesions in any tissues which were examined for nonperfused rats.

CONCLUSIONS

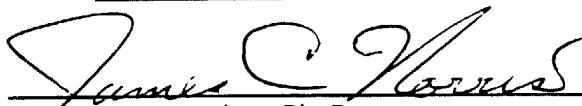
Exposure of vinyl pivalate vapor to rats for 2 weeks produced hypoactivity, no startle reflex, blepharospasm, and deep breathing which were noted during exposure to 500 and/or 1000 ppm. Clinical signs observed following exposures to 1000 ppm vinyl pivalate included incoordination, hypoactivity, increased incidence of swollen periocular tissue, periocular encrustation, and perinasal encrustation (females only). The incidence of periocular encrustation was also slightly increased in males from the 500 ppm group. Decreases in absolute body weight, body weight gain, and food consumption were observed in males and females from the 500 and/or 1000 ppm groups. Hematologic changes possibly indicative of anemia were observed in males from the 500 and 1000 ppm groups and females from all vinyl pivalate-exposed groups. Increases in liver and kidney weight were observed in males from the 1000 ppm group and in females from all vinyl pivalate-exposed groups. A decreased absolute brain weight was also noted for females from the 1000 ppm group.

Evidence for neurobehavioral alterations was noted in the 1000 ppm group, and the findings included an abnormal gait, decreased number of times the animal reared onto its hind legs (males), decreased forelimb grip strength, and increased landing hind leg splay. Various lesions were observed in the brain and spinal cords of all rats, both perfused and nonperfused, from the 1000 ppm group. In nonperfused rats, the lesions consisted of vacuolation and spongiosis in the brain stem (medulla and pons) and the ventral/lateral funiculi (white matter tracts) of the spinal cord. In perfused rats, the lesions included myelinopathy and axonopathy in the white matter of the pons and medulla oblongata, in the vestibular nuclei, midbrain, and trigeminal tracts, and in the ventral and lateral funiculi of the spinal cord.

Exposure of rats to 500 and 1000 ppm of vinyl pivalate vapor produced various clinical signs, hematologic changes suggestive of mild anemia, and effects on body weight, food consumption, and organ weights. Evidence of neurobehavioral alterations and microscopic lesions in the brain and spinal cord was noted for animals from the 1000 ppm group. Hematologic and organ weight changes were observed in females even at the lowest concentration (100 ppm). Thus, the no-observed-effect level (NOEL) of vinyl pivalate for males was considered to be 100 ppm under the conditions of this study. For females, a no-observed-adverse-effect level (NOAEL) was considered to be 100 ppm.

REVIEW AND APPROVAL

Study Director:


 James C. Norris, Ph.D.
2/10/95
Date

Senior Manager:


 Heather D. Buffleigh-Flayer, Ph.D.
2/10/95
Date

Director:


 John P. Van Miller, Ph.D., DABT
2/10/95
Date

KEY PERSONNEL

Study Director: James C. Norris

Technical Coordinator: P. J. Benson

Supervisors: L. C. Fisher
D. A. Neptun
E. V. Weaver

Scientists: P. E. Losco
D. A. Neptun
I. M. Pritts
J. D. Sun

Additional personnel are listed in the raw data.

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TABLE 1
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF CLINICAL OBSERVATIONS

CATEGORY FINDING (LOCATION)	GROUP: GRADE	MALES			
		1 (DAYS)	2 (DAYS)	3 (DAYS)	4 (DAYS)
PATE					
SCHEDULED SACRIFICE	P	5 (13)	5 (13)	5 (13)	5 (13)
SCHEDULED PERFUSION SACRIFICE	P	5 (11)	5 (11)	5 (11)	5 (11)
BEHAVIOR/CNS					
INCOORDINATION	P	0	0	0	10(2- 12)
ETES/EARS/NOSE					
PALE EYES (EYE-LEFT)	P	0	0	0	1 (4)
SWOLLEN PERIOCLULAR TISSUE (EYE-BOTH)	P	0	0	1 1(10- 11)	9 9(4- 10)
(EYE-LEFT)	P	0	0	0	1(4- 5)
(EYE-RIGHT)	P	0	0	0	2 (11)
PERIOCLULAR ENCRUSTATION (EYE-BOTH)	P	0	1	4	8
(EYE-LEFT)	P	0	0	1 (12)	3(4- 13)
	P	0	0	3(10- 13)	2(4- 8)

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

Grades: P = present, 1 = mild, 2 = moderate, 3 = severe.
Numbers represent the number of animals exhibiting the finding at least once during the study.
Parenthetical numbers "()" represent earliest to latest day a finding of the specified grade was observed.

TABLE 1 (Continued)
 VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
 SUMMARY OF CLINICAL OBSERVATIONS

CATEGORY FINDING (LOCATION)	GROUP: GRADE	MALES			
		1 (DAYS)	2 (DAYS)	3 (DAYS)	4 (DAYS)
EYES/EARS/NOSE					
PERIOcular ENCRUSTATION (CONTINUED)					
(EYE-RIGHT)	P	0	1 (11- 13)	0	5 (4- 13)
PERINASAL ENCRUSTATION	P	4 (11- 13)	1 (12- 13)	5 (11- 13)	0
PROCEDURAL TRAUMA					
(EYE-LEFT)	P	2 (11)	0	3	3
(EYE-RIGHT)	P	0	0	0	3 (11- 13)

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

Grades: P = present, 1 = mild, 2 = moderate, 3 = severe.
 Numbers represent the number of animals exhibiting the finding at least once during the study.
 Parenthetical numbers "()" represent earliest to latest day a finding of the specified grade was observed.

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TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF CLINICAL OBSERVATIONS

CATEGORY FINDING (LOCATION)	GROUP GRADE	FEMALES			
		1 (DAYS)	2 (DAYS)	3 (DAYS)	4 (DAYS)
FATE					
SCHEDULED SACRIFICE	P	5 (13)	5 (13)	5 (13)	5 (13)
SCHEDULED PERFUSION SACRIFICE	P	5 (12)	5 (12)	5 (12)	5 (12)
BEHAVIOR/CNS					
HYPOACTIVE	P	0	0	0	2 (11)
INCOORDINATION	P	0	0	0	10(2- 13)
BOOY					
URINE STAINS	P	1 (12)	0	0	0
EYES/EARS/NOSE					
SWOLLEN PERIOCLAR TISSUE (EYE-BOTH)	P	1 0	1 0	0 0	10 10(4- 10)
(EYE-LEFT)	P	0	0	0	2(12- 13)
(EYE-RIGHT)	P	1 (12)	1 (13)	0	0
PERIOCLAR ENCRUSTATION		0	1	2	6

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

Grades: P = present, 1 = mild, 2 = moderate, 3 = severe.
Numbers represent the number of animals exhibiting the finding at least once during the study.
Parenthetical numbers "()" represent earliest to latest day a finding of the specified grade was observed.

TABLE 2 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF CLINICAL OBSERVATIONS

FEMALES

CATEGORY FINDING (LOCATION)	GROUP: GRADE	1 (DAYS)	2 (DAYS)	3 (DAYS)	4 (DAYS)
EYES/EARS/NOSE					
PERIOcular ENCRUSTATION (CONTINUED)					
(EYE-BOTH)	P	0	0	0	2 (5)
(EYE-LEFT)	P	0	1 (12)	0	4 (8- 13)
(EYE-RIGHT)	P	0	0	2 (12- 13)	1 (13)
PERINASAL ENCRUSTATION	P	0	1 (12)	0	3 (12- 13)
PROCEDURAL TRAUMA					
(EYE-LEFT)	P	4	5	3	4
(EYE-RIGHT)	P	0	5 (12- 13)	0	4 (12- 13)
	P	4 (12)	0	3 (12- 13)	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

Grades: P = present, 1 = mild, 2 = moderate, 3 = severe.

Numbers represent the number of animals exhibiting the finding at least once during the study.

Parenthetical numbers "{}" represent earliest to latest day a finding of the specified grade was observed.

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TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF BODY WEIGHT (GRAMS)

MALES				
GROUP: PPM	0	100	500	1000
DAY 1				
MEAN	161.4	162.4	162.4	163.8
S.D.	12.18	10.93	10.62	8.83
N	10	10	10	10
DAY 2				
MEAN	165.5	164.4	164.7	167.6
S.D.	12.39	11.31	10.06	10.07
N	10	10	10	10
DAY 5				
MEAN	172.9	172.3	172.1	166.5
S.D.	13.31	12.27	10.61	11.38
N	10	10	10	10
DAY 8				
MEAN	181.6	181.0	182.4	174.0
S.D.	14.10	13.16	12.74	11.53
N	10	10	10	10
DAY 9				
MEAN	186.0	184.2	185.4	175.2
S.D.	14.35	12.88	12.49	14.80
N	10	10	10	10
DAY 12				
MEAN	190.1	184.2	184.5	175.4
S.D.	15.28	11.23	15.20	13.59
N	5	5	5	5
None significantly different from control group				

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF BODY WEIGHT GAIN (GRAMS)

MALES				
GROUP: PPM	0	100	500	1000
DAY 1 TO 2				
MEAN	4.1	1.9**	2.2*	3.7
S.D.	1.43	1.12	2.21	1.81
N	10	10	10	10
DAY 2 TO 5				
MEAN	7.4	7.9	7.5	-1.1**
S.D.	2.45	2.59	2.24	4.69
N	10	10	10	10
DAY 5 TO 8				
MEAN	8.7	8.7	10.2	7.5
S.D.	1.51	1.54	3.18	3.01
N	10	10	10	10
DAY 8 TO 9				
MEAN	4.4	3.2	3.0	1.2
S.D.	0.85	0.84	1.59	4.97
N	10	10	10	10
DAY 9 TO 12				
MEAN	2.4	3.0	-4.0	-2.4*
S.D.	2.59	2.61	6.04	2.44
N	5	5	5	5
* Significantly different from control group (p < .05)				
** Significantly different from control group (p < .01)				

TABLE 5
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF BODY WEIGHT (GRAMS)

FEMALES				
GROUP: PPM	0	100	500	1000
DAY 1				
MEAN	125.3	125.8	126.9	125.1
S.D.	6.65	8.82	4.73	7.80
N	10	10	10	10
DAY 2				
MEAN	127.7	129.0	127.0	127.6
S.D.	6.05	7.68	5.21	6.54
N	10	10	10	10
DAY 5				
MEAN	130.3	132.6	129.6	123.5*
S.D.	5.89	8.17	4.94	6.40
N	10	10	10	10
DAY 8				
MEAN	134.2	137.9	132.9	125.6**
S.D.	4.76	7.88	5.68	6.50
N	10	10	10	10
DAY 9				
MEAN	136.5	140.2	132.9	127.0**
S.D.	5.68	8.15	5.67	7.50
N	10	10	10	10
DAY 12				
MEAN	134.5	137.2	133.0	125.7*
S.D.	5.52	5.04	4.23	6.51
N	5	5	5	5
* Significantly different from control group (p < .05)				
** Significantly different from control group (p < .01)				

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF BODY WEIGHT GAIN (GRAMS)

FEMALES				
GROUP: PPM	0	100	500	1000
DAY 1 TO 2				
MEAN	2.4	3.2	0.1*	2.5
S.D.	2.06	2.44	1.73	2.58
N	10	10	10	10
DAY 2 TO 5				
MEAN	2.6	3.7	2.5	-4.1**
S.D.	2.35	2.00	2.16	2.59
N	10	10	10	10
DAY 5 TO 8				
MEAN	3.9	5.3	3.3	2.0
S.D.	2.78	2.32	1.57	1.62
N	10	10	10	10
DAY 8 TO 9				
MEAN	2.3	2.3	0.1	1.4
S.D.	2.41	2.38	2.61	1.32
N	10	10	10	10
DAY 9 TO 12				
MEAN	-2.4	-2.5	0.1	-2.6
S.D.	2.74	2.70	3.76	2.68
N	5	5	5	5
* Significantly different from control group (p < .05)				
** Significantly different from control group (p < .01)				

TABLE 7
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

MALES				
GROUP: PPM	0	100	500	1000
DAY 1 TO 5				
MEAN	15.1	14.6	14.4	10.7**
S.D.	1.17	1.33	0.78	0.93
N	10	10	10	10
DAY 5 TO 8				
MEAN	16.6	16.8	17.4	17.1
S.D.	1.34	1.39	1.19	1.59
N	10	10	10	10
DAY 8 TO 10				
MEAN	14.7	13.9	13.5*	11.1**
S.D.	1.16	1.18	1.05	1.97
N	10	10	10	10
* Significantly different from control group (p < .05)				
** Significantly different from control group (p < .01)				

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

FEMALES				
GROUP: PPM	0	100	500	1000
DAY 1 TO 5				
MEAN	11.1	11.0	10.1**	9.3**
S.D.	0.30	0.63	1.07	0.56
N	10	10	10	10
DAY 5 TO 8				
MEAN	11.8	13.2**	12.4	12.2
S.D.	0.50	0.77	0.99	0.66
N	10	10	10	10
DAY 8 TO 10				
MEAN	11.4	11.6	10.6*	9.1**
S.D.	0.77	0.79	0.98	0.67
N	10	10	10	10
* Significantly different from control group (p < .05)				
** Significantly different from control group (p < .01)				

TABLE 9
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 10

MALES				
GROUP: PPM	0	100	500	1000
ERYTHROCYTES ($10^6/\mu\text{l}$)				
MEAN	7.82	7.71	7.43**	7.27**
S.D.	0.166	0.199	0.305	0.217
N	10	10	10	10
HEMOGLOBIN (g/dl)				
MEAN	15.2	15.1	14.4**	13.7**
S.D.	0.28	0.36	0.50	0.35
N	10	10	10	10
HEMATOCRIT (%)				
MEAN	43.7	43.1	41.6**	40.2**
S.D.	0.76	0.95	1.37	1.35
N	10	10	10	10
MEAN CORPUSCULAR VOLUME (μm^3)				
MEAN	56.	56.	56.	55.
S.D.	0.6	0.5	0.8	0.5
N	10	10	10	10
MEAN CORPUSCULAR HEMOGLOBIN (pg)				
MEAN	19.4	19.6	19.4	18.8**
S.D.	0.21	0.27	0.29	0.24
N	10	10	10	10
MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)				
MEAN	34.7	35.0	34.6	34.0**
S.D.	0.43	0.37	0.38	0.50
N	10	10	10	10
PLATELETS ($10^3/\mu\text{l}$)				
MEAN	663.	633.	636.	745.**
S.D.	35.5	49.7	44.0	60.7
N	9	10	9	9
LEUKOCYTES ($10^3/\mu\text{l}$)				
MEAN	6.2	6.5	6.1	7.3*
S.D.	1.18	0.38	0.16	0.73
N	10	10	10	10
SEGMENTED NEUTROPHILS ($10^3/\mu\text{l}$)				
MEAN	0.61	0.54	0.49	0.57
S.D.	0.367	0.103	0.107	0.174
N	10	10	10	10
LYMPHOCYTES ($10^3/\mu\text{l}$)				
MEAN	5.39	5.76	5.50	6.53**
S.D.	0.815	0.347	0.175	0.607
N	10	10	10	10
MONOCYTES ($10^3/\mu\text{l}$)				
MEAN	0.04	0.08	0.03	0.06
S.D.	0.033	0.097	0.052	0.094
N	10	10	10	10

* Significantly different from control group ($p < .05$)

** Significantly different from control group ($p < .01$)

TABLE 9 (continued)
 VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
 SUMMARY OF HEMATOLOGY
 DAY 10

MALES				
GROUP: PPM	0	100	500	1000
BASOPHILS ($10^3/\mu\text{l}$)				
MEAN	0.07	0.05	0.07	0.07
S.D.	0.028	0.029	0.028	0.033
N	10	10	10	10
EOSINOPHILS ($10^3/\mu\text{l}$)				
MEAN	0.05	0.03	0.06	0.04
S.D.	0.054	0.015	0.049	0.018
N	10	10	10	10
BANDED NEUTROPHILS ($10^3/\mu\text{l}$)				
MEAN		0.00	0.00	0.00
S.D.		0.000	0.000	0.000
N		1	1	1
LARGE MONONUCLEAR CELLS ($10^3/\mu\text{l}$)				
MEAN		0.00	0.00	0.00
S.D.		0.000	0.000	0.000
N		1	1	1
LARGE GRANULAR LYMPHOCYTES ($10^3/\mu\text{l}$)				
MEAN		0.00	0.00	0.00
S.D.		0.000	0.000	0.000
N		1	1	1
IMMATURE GRANULOCYTES ($10^3/\mu\text{l}$)				
MEAN		0.00	0.00	0.00
S.D.		0.000	0.000	0.000
N		1	1	1
NUCLEATED RBCs (cells/100 WBCs)				
MEAN		1.	7.	4.
S.D.		0.0	0.0	0.0
N		1	1	1
None significantly different from control group				

TABLE 10
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 11

FEMALES				
GROUP: PPM	0	100	500	1000
ERYTHROCYTES ($10^6/\mu\text{l}$)				
MEAN	7.81	7.51**	7.39**	7.39**
S.D.	0.237	0.167	0.144	0.285
N	9	10	10	10
HEMOGLOBIN (g/dl)				
MEAN	15.4	15.0*	14.4**	14.1**
S.D.	0.47	0.20	0.23	0.50
N	9	10	10	10
HEMATOCRIT (%)				
MEAN	43.2	41.6**	40.9**	40.5**
S.D.	1.25	0.76	0.75	1.78
N	9	10	10	10
MEAN CORPUSCULAR VOLUME (μm^3)				
MEAN	55.	55.	55.	55.
S.D.	0.5	0.5	0.5	0.6
N	9	10	10	10
MEAN CORPUSCULAR HEMOGLOBIN (pg)				
MEAN	19.7	19.9	19.5	19.0**
S.D.	0.28	0.38	0.40	0.24
N	9	10	10	10
MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)				
MEAN	35.6	36.0	35.3	34.7**
S.D.	0.75	0.50	0.75	0.59
N	9	10	10	10
PLATELETS ($10^3/\mu\text{l}$)				
MEAN	625.	617.	649.	677.
S.D.	31.1	58.1	67.5	64.7
N	9	10	7	10
LEUKOCYTES ($10^3/\mu\text{l}$)				
MEAN	7.5	6.7	8.2	6.7
S.D.	0.93	0.74	0.88	1.19
N	9	10	10	10
SEGMENTED NEUTROPHILS ($10^3/\mu\text{l}$)				
MEAN	0.70	0.66	0.82	0.73
S.D.	0.195	0.215	0.224	0.235
N	9	10	10	10
LYMPHOCYTES ($10^3/\mu\text{l}$)				
MEAN	6.64	5.91	7.22	5.81*
S.D.	0.751	0.593	0.678	1.054
N	9	10	10	10
MONOCYTES ($10^3/\mu\text{l}$)				
MEAN	0.04	0.07	0.04	0.07
S.D.	0.033	0.084	0.017	0.065
N	9	10	10	10

* Significantly different from control group ($p < .05$)

** Significantly different from control group ($p < .01$)

TABLE 10 (continued)
 VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
 SUMMARY OF HEMATOLOGY
 DAY 11

FEMALES				
GROUP: PPM	0	100	500	1000
BASOPHILS ($10^3/\mu\text{l}$)				
MEAN	0.07	0.05*	0.07	0.03**
S.D.	0.022	0.021	0.019	0.027
N	9	10	10	10
EOSINOPHILS ($10^3/\mu\text{l}$)				
MEAN	0.04	0.05	0.08	0.06
S.D.	0.011	0.055	0.045	0.063
N	9	10	10	10
BANDIED NEUTROPHILS ($10^3/\mu\text{l}$)				
MEAN		0.00		0.00
S.D.		0.000		0.000
N		1		3
LARGE MONONUCLEAR CELLS ($10^3/\mu\text{l}$)				
MEAN		0.00		0.00
S.D.		0.000		0.000
N		1		3
LARGE GRANULAR LYMPHOCYTES ($10^3/\mu\text{l}$)				
MEAN		0.00		0.00
S.D.		0.000		0.000
N		1		3
IMMATURE GRANULOCYTES ($10^3/\mu\text{l}$)				
MEAN		0.00		0.00
S.D.		0.000		0.000
N		1		3
NUCLEATED RBCs (cells/100 WBCs)				
MEAN		0.		2.
S.D.		0.0		1.5
N		1		3
* Significantly different from control group (p < .05)				
** Significantly different from control group (p < .01)				

TABLE 11
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
PREEXPOSURE

MALES				
GROUP: (PPM)	0	100	500	1000
Cage Posture				
Normal/awake	5	7	8	5
Normal/asleep	5	3	2	5
Cage Palpebral Closure				
Wide open	3	5	6	3
Slight droop	1	0	0	1
Halfway shut	1	2	2	1
Shut	5	3	2	5
Defecation				
None	8	8	7	8
Normal	2	2	3	2
Urine				
None	7	7	7	8
Present	3	3	3	2
Rears (events)				
MEAN	14.10	12.00	12.20	14.50
S.D.	8.279	5.637	5.574	5.874
N	10	10	10	10
Grip Strength (fore) (kg)				
MEAN	.54	.50	.52	.53
S.D.	.080	.085	.087	.108
N	10	10	10	10
Grip Strength (hind) (kg)				
MEAN	.29	.27	.30	.28
S.D.	.033	.049	.059	.067
N	10	10	10	10
Body Temperature (degrees C)				
MEAN	38.05	38.02	38.02	38.15
S.D.	.280	.155	.278	.375
N	10	10	10	10
Body Weight (grams)				
MEAN	143.19	143.51	143.82	143.63
S.D.	9.087	9.055	8.501	6.727
N	10	10	10	10
None significantly different from control group				

TABLE 11
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
PREEXPOSURE

MALES

GROUP: (PPM)	0	100	500	1000
Hind Leg Splay (cm)				
MEAN	3.96	3.88	3.88	4.05
S.D.	1.060	.531	1.241	.541
N	10	10	10	10

None significantly different from control group

All tested animals exhibited the same finding(s) for the following parameter(s):
Cage Twitch, Cage Tremor, Cage Spasm, Cage Jerk, Cage Clonic Convulsions,
Cage Tonic Convulsions, Handling Reactivity, Ataxia, Gait, Body Position,
Excessive Vocalization, Breathing Pattern, Twitch, Tremor, Spasm, Jerk,
Clonic Convulsions, Tonic Convulsions, Unusual Behavior, Arousal, Palpebral
Closure, Piloerection, Approach Response, Startle Response, Tail Pinch
Response, Pupil Size, Muscle Tone, Lacrimation, Salivation, Fur Appearance,
Facial Crust, Additional Observations, Visual Placing, Air Righting

Statistical analysis of grip strength and hind leg splay values was performed
for all tests combined, not for individual tests. Details of the statistical
analysis can be found in the raw data. No statistical analysis was performed
for non-continuous parameters in which the same finding was entered for all
animals in the control group and for all animals in the dose group being examined.

RPT_NT:VPTRMF1.SFO

TABLE 12
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS DAY 10				
MALES				
GROUP: (PPM)	0	100	500	1000
Cage Posture				
Normal/awake	8	8	6	4
Normal/asleep	2	2	4	6
Cage Palpebral Closure				
Wide open	5	2	3	3
Slight droop	2	4	1	0
Halfway shut	1	2	2	1
Shut	2	2	4	6
Ataxia				
No	10	10	10	9
Yes				
Present	0	0	0	1
Gait				
Normal	10	9	10	1**
Uncoordinated				
Present	0	1	0	9
Unusual Behavior				
None	10	9	10	10
Other	0	1 ^a	0	0
Arousal				
Active	9	7	7	9
Hyperactive	0	0	1	0
Inactive/alert	1	3	2	1
Palpebral Closure				
Wide open	10	9	9	9
Slight droop	0	1	1	1
Defecation				
None	10	9	9	9
Normal	0	1	1	1
Urine				
None	9	9	8	10
Present	1	1	2	0
Rears (events)				
MEAN	7.90	8.80	11.20	6.20
S.D.	3.900	6.925	10.185	3.048
N	10	10	10	10
Pupil Size				
Normal	10	10	10	9
Decreased	0	0	0	1

**Significantly different from control group (p < 0.01)

^a Continuous slight head tilt to the left while in arena

TABLE 12
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS DAY 10				
MALES				
GROUP: (PPM)	0	100	500	1000
Grip Strength (fore) (kg)				
MEAN	.68	.66	.65	.51**
S.D.	.075	.109	.131	.104
N	* 10	10	10	10
Grip Strength (hind) (kg)				
MEAN	.39	.34	.37	.34
S.D.	.064	.068	.055	.037
N	10	10	10	10
Body Temperature (degrees C)				
MEAN	38.10	38.05	38.06	37.82
S.D.	.368	.453	.477	.365
N	10	10	10	10
Body Weight (grams)				
MEAN	185.65	183.61	184.75	175.65
S.D.	14.531	12.958	13.091	12.021
N	10	10	10	10
Air Righting				
Feet/coordinated	10	10	10	9
Back	0	0	0	1
Hind Leg Splay (cm)				
MEAN	4.42	4.16	4.62	7.72**
S.D.	.705	.506	.867	1.275
N	10	10	10	10
**Significantly different from control group (p < 0.01)				

All tested animals exhibited the same finding(s) for the following parameter(s):
Cage Twitch, Cage Tremor, Cage Spasm, Cage Jerk, Cage Clonic Convulsions,
Cage Tonic Convulsions, Handling Reactivity, Body Position, Excessive
Vocalization, Breathing Pattern, Twitch, Tremor, Spasm, Jerk, Clonic
Convulsions, Tonic Convulsions, Piloerection, Approach Response, Startle
Response, Tail Pinch Response, Muscle Tone, Lacrimation, Salivation, Fur
Appearance, Facial Crust, Additional Observations, Visual Placing

Statistical analysis of grip strength and hind leg splay values was performed
for all tests combined, not for individual tests. Details of the statistical
analysis can be found in the raw data. No statistical analysis was performed
for non-continuous parameters in which the same finding was entered for all
animals in the control group and for all animals in the dose group being examined.

RPT_NT:VPTRMF2.SFO

TABLE 13
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS PREEXPOSURE				
FEMALES				
GROUP: (PPM)	0	100	500	1000
Cage Posture				
Normal/awake	7	7	8	6
Normal/asleep	3	3	2	4
Cage Palpebral Closure				
Wide open	5	4	4	5
Slight droop	0	0	1	0
Halfway shut	2	3	3	1
Shut	3	3	2	4
Arousal				
Active	9	10	10	10
Inactive/alert	1	0	0	0
Defecation				
None	8	9	8	10
Normal	2	1	2	0
Urine				
None	6	8	5	5
Present	4	2	5	5
Rears (events)				
MEAN	14.30	17.10	19.10	15.10
S.D.	7.804	4.408	6.367	5.087
N	10	10	10	10
Startle Response				
Noticeable reaction	10	10	9	10
Exaggerated reaction	0	0	1	0
Grip Strength (fore) (kg)				
MEAN	.55	.53	.50	.57
S.D.	.096	.077	.066	.071
N	10	10	10	10
Grip Strength (hind) (kg)				
MEAN	.25	.31	.29	.30
S.D.	.035	.053	.047	.069
N	10	10	10	10
Body Temperature (degrees C)				
MEAN	37.81	37.90	37.81	37.75
S.D.	.375	.267	.260	.232
N	10	10	10	10
Body Weight (grams)				
MEAN	121.02	121.80	119.40	121.10
S.D.	7.311	7.582	5.347	6.318
N	10	10	10	10
None significantly different from control group				

TABLE 13
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
PREEXPOSURE

FEMALES

GROUP: (PPM)	0	100	500	1000
Hind Leg Splay (cm)				
MEAN	3.38	3.45	3.59	3.06
S.D.	.749	.425	.653	.558
N	10	10	10	10

None significantly different from control group

All tested animals exhibited the same finding(s) for the following parameter(s):
Cage Twitch, Cage Tremor, Cage Spasm, Cage Jerk, Cage Clonic Convulsions,
Cage Tonic Convulsions, Handling Reactivity, Ataxia, Gait, Body Position,
Excessive Vocalization, Breathing Pattern, Twitch, Tremor, Spasm, Jerk,
Clonic Convulsions, Tonic Convulsions, Unusual Behavior, Palpebral Closure,
Piloerection, Approach Response, Tail Pinch Response, Pupil Size, Muscle
Tone, Lacrimation, Salivation, Fur Appearance, Facial Crust, Additional
Observations, Visual Placing, Air Righting

Statistical analysis of grip strength and hind leg splay values was performed
for all tests combined, not for individual tests. Details of the statistical
analysis can be found in the raw data. No statistical analysis was performed
for non-continuous parameters in which the same finding was entered for all
animals in the control group and for all animals in the dose group being examined.

RPT_NT:VPTRFF1.SFO

TABLE 14
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 11

FEMALES

GROUP: (PPM)	0	100	500	1000
Cage Palpebral Closure				
Wide open	10	10	9	7
Slight droop	0	0	0	1
Halfway shut	0	0	1	2
Ataxia				
No	10	10	10	9
Yes				
Present	0	0	0	1
Gait				
Normal	10	10	10	0**
Uncoordinated				
Present	0	0	0	9
Other				
Present	0	0	0	1 ^a
Arousal				
Active	9	8	10	8
Hyperactive	0	0	0	1
Inactive/alert	1	2	0	1
Palpebral Closure				
Wide open	9	10	10	10
Slight droop	1	0	0	0
Defecation				
None	9	10	10	10
Normal	1	0	0	0
Urine				
None	8	10	9	9
Present	2	0	1	1
Rears (events)				
MEAN	13.10	12.20	15.80	12.10
S.D.	7.534	7.786	9.090	8.130
N	10	10	10	10
Pupil Size				
Normal	9	9	10	10
Increased	0	1 ^b	0	0
Decreased	1	0	0	0

**Significantly different from control group ($p < 0.01$)

^a Slight wobble in rear quarters when walking

^b Right pupil size was increased while the left pupil size was normal

TABLE 14
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF FUNCTIONAL OBSERVATIONS
DAY 11

FEMALES

GROUP: (PPM)	0	100	500	1000
Grip Strength (fore) (kg)				
MEAN	.63	.57	.57	.46**
S.D.	.086	.110	.093	.145
N	10	10	10	10
Grip Strength (hind) (kg)				
MEAN	.34	.34	.33	.32
S.D.	.064	.055	.038	.059
N	10	10	10	10
Body Temperature (degrees C)				
MEAN	38.02	38.33	38.10	38.00
S.D.	.464	.427	.383	.548
N	10	10	10	10
Body Weight (grams)				
MEAN	137.43	141.33	135.13	127.03**
S.D.	5.398	7.553	5.243	6.108
N	10	10	10	10
Air Righting				
Feet/coordinated	10	10	9	10
Side	0	0	1	0
Hind Leg Splay (cm)				
MEAN	3.49	3.26	3.90	7.42**
S.D.	.422	.370	.952	.865
N	10	10	10	10

**Significantly different from control group (p < 0.01)

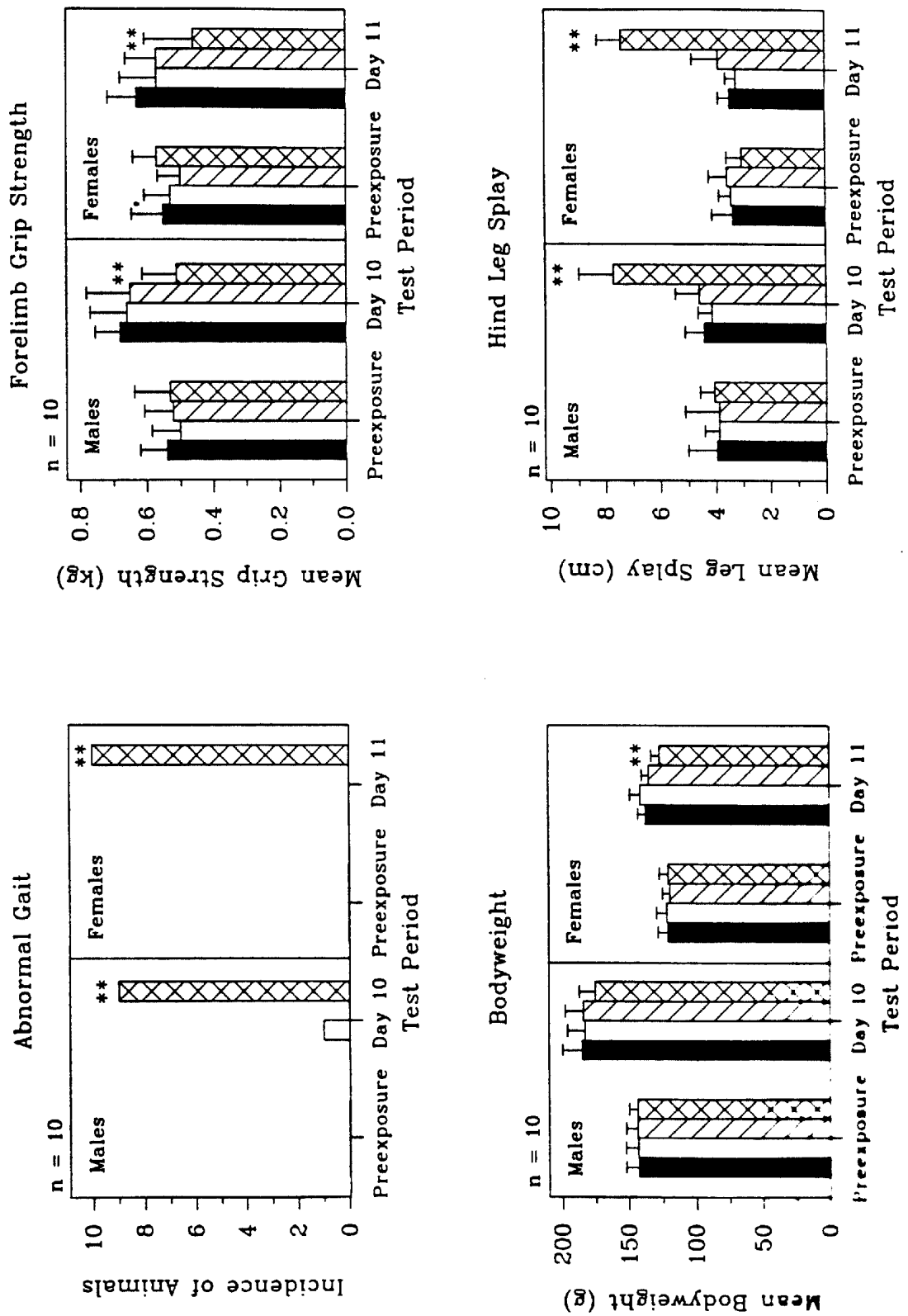
All tested animals exhibited the same finding(s) for the following parameter(s):
Cage Posture, Cage Twitch, Cage Tremor, Cage Spasm, Cage Jerk, Cage Clonic
Convulsions, Cage Tonic Convulsions, Handling Reactivity, Body Position,
Excessive Vocalization, Breathing Pattern, Twitch, Tremor, Spasm, Jerk,
Clonic Convulsions, Tonic Convulsions, Unusual Behavior, Piloerection,
Approach Response, Startle Response, Tail Pinch Response, Muscle Tone,
Lacrimation, Salivation, Fur Appearance, Facial Crust, Additional
Observations, Visual Placing

Statistical analysis of grip strength and hind leg splay values was performed
for all tests combined, not for individual tests. Details of the statistical
analysis can be found in the raw data. No statistical analysis was performed
for non-continuous parameters in which the same finding was entered for all
animals in the control group and for all animals in the dose group being examined.

RPT_NT:VPTRFF2.SFO

FIGURE 1
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
GRAPHS OF SELECTED FUNCTIONAL OBSERVATIONAL BATTERY PARAMETERS AT EACH TEST SESSION

EXPOSURE GROUPS: ■ - 0 PPM; □ - 100 PPM; ▨ - 500 PPM; ▩ - 1000 PPM



** Significantly different from control group (p < 0.01)

TABLE 15
 VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
 SUMMARY OF ORGAN WEIGHTS (GRAMS)
 ANIMALS SACRIFICED AT DAY 13

MALES				
GROUP: PPM	0	100	500	1000
FINAL BODY WEIGHT				
MEAN	195.5	186.3	189.0	181.9
S.D.	15.26	11.10	15.20	14.46
N	5	5	5	5
LIVER				
MEAN	8.730	8.242	8.920	10.331*
S.D.	0.8643	0.5112	1.0590	1.1224
N	5	5	5	5
KIDNEYS				
MEAN	1.584	1.530	1.605	1.666
S.D.	0.1645	0.0652	0.1180	0.1354
N	5	5	5	5
LUNGS				
MEAN	0.965	0.898	0.910	0.963
S.D.	0.0915	0.0663	0.0577	0.0929
N	5	5	5	5
SPLEEN				
MEAN	0.480	0.472	0.481	0.447
S.D.	0.0365	0.0232	0.0424	0.0499
N	5	5	5	5
HEART				
MEAN	0.688	0.663	0.692	0.720
S.D.	0.0645	0.0624	0.0298	0.0688
N	5	5	5	5
BRAIN				
MEAN	1.774	1.760	1.728	1.706
S.D.	0.0572	0.0319	0.0490	0.0429
N	5	5	5	5
ADRENAL GL				
MEAN	0.042	0.043	0.040	0.045
S.D.	0.0027	0.0092	0.0074	0.0105
N	5	5	5	5
TESTES				
MEAN	2.391	2.196	2.447	2.209
S.D.	0.2638	0.3475	0.2071	0.2022
N	5	5	5	5
* Significantly different from control group (p < .05)				

TABLE 16
 VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
 SUMMARY OF ORGAN WEIGHTS (GRAMS)
 ANIMALS SACRIFICED AT DAY 13

FEMALES				
GROUP: PPM	0	100	500	1000
FINAL BODY WEIGHT				
MEAN	138.1	139.3	136.2	127.9
S.D.	5.21	6.86	5.06	8.55
N	5	5	5	5
LIVER				
MEAN	5.284	5.755	6.093**	6.414**
S.D.	0.2113	0.3770	0.2166	0.5746
N	5	5	5	5
KIDNEYS				
MEAN	1.109	1.191	1.189	1.144
S.D.	0.0550	0.0579	0.0273	0.0542
N	5	5	5	5
LUNGS				
MEAN	0.846	0.827	0.843	0.811
S.D.	0.0573	0.0390	0.0607	0.0492
N	5	5	5	5
SPLEEN				
MEAN	0.410	0.427	0.435	0.374
S.D.	0.0206	0.0473	0.0176	0.0644
N	5	5	5	5
HEART				
MEAN	0.538	0.565	0.567	0.572
S.D.	0.0326	0.0315	0.0319	0.0513
N	5	5	5	5
BRAIN				
MEAN	1.656	1.685	1.658	1.572*
S.D.	0.0436	0.0438	0.0263	0.0678
N	5	5	5	5
ADRENAL GL				
MEAN	0.045	0.050	0.045	0.048
S.D.	0.0044	0.0047	0.0058	0.0060
N	5	5	5	5
OVARIES				
MEAN	0.093	0.101	0.100	0.094
S.D.	0.0130	0.0144	0.0136	0.0184
N	5	5	5	5

* Significantly different from control group ($p < .05$)

** Significantly different from control group ($p < .01$)

TABLE 17
 VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
 SUMMARY OF ORGAN WEIGHTS AS % OF FINAL BODY WEIGHT
 ANIMALS SACRIFICED AT DAY 13

MALES				
GROUP: PPM	0	100	500	1000
LIVER				
MEAN	4.461	4.423	4.708	5.671**
S.D.	0.1905	0.0286	0.2251	0.2704
N	5	5	5	5
KIDNEYS				
MEAN	0.809	0.822	0.850*	0.916**
S.D.	0.0328	0.0197	0.0141	0.0179
N	5	5	5	5
LUNGS				
MEAN	0.494	0.482	0.483	0.529
S.D.	0.0399	0.0259	0.0323	0.0303
N	5	5	5	5
SPLEEN				
MEAN	0.246	0.254	0.255	0.246
S.D.	0.0148	0.0090	0.0152	0.0201
N	5	5	5	5
HEART				
MEAN	0.351	0.356	0.368	0.396**
S.D.	0.0105	0.0285	0.0317	0.0148
N	5	5	5	5
BRAIN				
MEAN	0.910	0.947	0.920	0.942
S.D.	0.0596	0.0461	0.0894	0.0724
N	5	5	5	5
ADRENAL GL				
MEAN	0.022	0.023	0.022	0.024
S.D.	0.0019	0.0040	0.0044	0.0047
N	5	5	5	5
TESTES				
MEAN	1.221	1.175	1.295	1.216
S.D.	0.0680	0.1372	0.0179	0.0946
N	5	5	5	5

* Significantly different from control group ($p < .05$)

** Significantly different from control group ($p < .01$)

TABLE 18
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF ORGAN WEIGHTS AS % OF FINAL BODY WEIGHT
ANIMALS SACRIFICED AT DAY 13

FEMALES				
GROUP: PPM	0	100	500	1000
LIVER				
MEAN	3.828	4.131**	4.473**	5.012**
S.D.	0.1227	0.1268	0.0329	0.2580
N	5	5	5	5
KIDNEYS				
MEAN	0.803	0.856*	0.874**	0.895**
S.D.	0.0312	0.0196	0.0409	0.0271
N	5	5	5	5
LUNGS				
MEAN	0.614	0.594	0.620	0.634
S.D.	0.0546	0.0298	0.0515	0.0286
N	5	5	5	5
SPLEEN				
MEAN	0.298	0.306	0.319	0.293
S.D.	0.0245	0.0253	0.0093	0.0562
N	5	5	5	5
HEART				
MEAN	0.390	0.405	0.416	0.450
S.D.	0.0250	0.0087	0.0115	0.0626
N	5	5	5	5
BRAIN				
MEAN	1.200	1.211	1.219	1.231
S.D.	0.0239	0.0414	0.0549	0.0508
N	5	5	5	5
ADRENAL GL				
MEAN	0.033	0.036	0.033	0.037
S.D.	0.0026	0.0040	0.0043	0.0055
N	5	5	5	5
OVARIES				
MEAN	0.067	0.073	0.073	0.073
S.D.	0.0089	0.0089	0.0092	0.0105
N	5	5	5	5
* Significantly different from control group (p < .05)				
** Significantly different from control group (p < .01)				

TABLE 19
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF ORGAN WEIGHTS AS % OF BRAIN WEIGHT
ANIMALS SACRIFICED AT DAY 13

MALES				
GROUP: PPM	0	100	500	1000
LIVER				
MEAN	492.226	468.064	516.766	605.391**
S.D.	46.3093	23.6813	66.8659	63.9536
N	5	5	5	5
KIDNEYS				
MEAN	89.307	86.924	92.934	97.578
S.D.	8.4491	3.4188	7.5506	7.1463
N	5	5	5	5
LUNGS				
MEAN	54.424	51.017	52.634	56.371
S.D.	5.1870	3.6777	2.9193	4.6268
N	5	5	5	5
SPLEEN				
MEAN	27.069	26.836	27.838	26.183
S.D.	2.3036	1.1744	2.4538	2.9717
N	5	5	5	5
HEART				
MEAN	38.731	37.667	40.071	42.234
S.D.	2.7425	3.4995	1.6590	4.1957
N	5	5	5	5
ADRENAL GL				
MEAN	2.392	2.432	2.330	2.604
S.D.	0.1574	0.5281	0.3611	0.5579
N	5	5	5	5
TESTES				
MEAN	134.812	124.734	141.769	129.377
S.D.	14.2044	19.3085	13.9142	10.0534
N	5	5	5	5
** Significantly different from control group (p < .01)				

TABLE 20
 VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
 SUMMARY OF ORGAN WEIGHTS AS % OF BRAIN WEIGHT
 ANIMALS SACRIFICED AT DAY 13

FEMALES				
GROUP: PPM	0	100	500	1000
LIVER				
MEAN	319.147	341.347	367.611**	407.996**
S.D.	13.7861	14.2688	15.4645	31.7954
N	5	5	5	5
KIDNEYS				
MEAN	66.920	70.705*	71.744**	72.787**
S.D.	2.1527	2.5997	2.1779	2.5730
N	5	5	5	5
LUNGS				
MEAN	51.145	49.050	50.866	51.568
S.D.	4.1974	1.4915	3.5628	2.2626
N	5	5	5	5
SPLEEN				
MEAN	24.797	25.280	26.252	23.851
S.D.	1.7669	2.2208	1.4212	4.6362
N	5	5	5	5
HEART				
MEAN	32.474	33.504	34.202	36.424
S.D.	2.1806	1.4911	2.1991	3.7478
N	5	5	5	5
ADRENAL GL				
MEAN	2.738	2.980	2.724	3.039
S.D.	0.2094	0.2708	0.3211	0.3477
N	5	5	5	5
OVARIES				
MEAN	5.605	6.013	6.006	5.990
S.D.	0.8114	0.8041	0.8097	1.0188
N	5	5	5	5
* Significantly different from control group (p < .05)				
** Significantly different from control group (p < .01)				

TABLE 21
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		10	10	10	10
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
SKIN					
CRUST/SCAB/SCALE		2	2	3	3
SWOLLEN		0	0	0	1
LYMPH ND, S-MAN					
COLOR CHANGE, DIFFUSE		0	1	2	0
SKELETAL MUSCLE					
TRAUMATIZED		1	0	0	0
BRAIN					
MENINGEAL HEMORRHAGE		2	2	0	0
EYE					
TRAUMATIZED		0	0	2	1
LUNGS					
COLOR CHANGE, FOCAL/MULTIFOCAL		0	1	0	0
GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM					

TABLE 22
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		10	10	10	10
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
LIVER					
ANOMALY		0	1	0	0
SKIN					
SWOLLEN		1	1	0	2
CRUST/SCAB/SCALE		0	1	1	5
LYMPH ND, S-MAN					
COLOR CHANGE, FOCAL/MULTIFOCAL		2	1	1	2
COLOR CHANGE, DIFFUSE		1	2	2	2
SIZE INCREASE		1	0	0	0
LYMPH ND, OTHER					
SIZE INCREASE		1	0	0	0
THYMIC REGION					
COLOR CHANGE, FOCAL/MULTIFOCAL		4	2	2	0
BRAIN					
MENINGEAL HEMORRHAGE		1	0	0	0
EYE					
TRAUMATIZED		0	0	2	1
HARDERIAN GL					
COLOR CHANGE, DIFFUSE		0	0	0	1
OVARIES					
CYST		0	0	0	1
LUNGS					
COLOR CHANGE, FOCAL/MULTIFOCAL		1	0	0	0
GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM					

TABLE 23
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		5	5	5	5
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
SKIN					
CRUST/SCAB/SCALE		0	0	1	2
EYE					
TRAUMATIZED		0	0	1	0
GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM					

TABLE 24
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT DAY 12
PERFUSED FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		5	5	5	5
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
BRAIN, NOS					
MENINGEAL HEMORRHAGE •		0	1	0	0
SPINAL CORD, CRV					
HEMORRHAGE		1	0	0	0
SKIN					
SWOLLEN		0	0	0	1
EYE					
TRAUMATIZED		2	1	1	0
GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM					

TABLE 25
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	10	10	10	10
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
HEART				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
ORAL/PHARYNGEAL				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
STOMACH				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
LIVER				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
ADRENAL GL				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
SKIN				
TOTAL NUMBER EXAMINED	2	0	0	3
EXAMINED, UNREMARKABLE	2	-	-	2
SUBCUTANEOUS EDEMA	0	-	-	1
MODERATE	0	-	-	1
BLEPHARITIS	0	-	-	1
MODERATE	0	-	-	1
SPLEEN				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
SKELETAL MUSCLE				
TOTAL NUMBER EXAMINED	0	0	0	0
MISSING	1	-	-	-
BRAIN				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	3	4	4	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 25 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	10	10	10	10
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
BRAIN (CONTINUED)				
MENINGEAL HEMORRHAGE	0	1	0	0
MILD	0	1	0	0
BRAIN HEMORRHAGE	0	1	1	0
MINIMAL	0	1	0	0
MILD	0	0	1	0
VACUOLATION/SPONGIOSIS	2	0	0	5
MINIMAL	2	0	0	0
MILD	0	0	0	4
MODERATE	0	0	0	1
SPINAL CORD				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	0
VACUOLATION/SPONGIOSIS	0	0	0	5**
MODERATE	0	0	0	3
MARKED	0	0	0	2
AXON DEGENERATION/FRAGMENTATION	0	0	0	1
MODERATE	0	0	0	1
NERVE, SCIATIC				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
EYE				
TOTAL NUMBER EXAMINED	0	0	0	1
CONJUNCTIVITIS	-	-	-	1
MARKED	-	-	-	1

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

** Significantly different from control group (p < .01)

TABLE 25 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	10	10	10	10
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
EYE (CONTINUED)				
HYPHEMA/HEMORRHAGE	-	-	-	1
MODERATE	-	-	-	1
KERATITIS	-	-	-	1
MARKED	-	-	-	1
CORNEAL ULCER	-	-	-	1
MARKED	-	-	-	1
HYPOPYON	-	-	-	1
MARKED	-	-	-	1
TESTES				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
NASAL CAVITY				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	4
DACRYOSOLENITIS	0	-	-	1
MILD	0	-	-	1
LARYNX				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
TRACHEA				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	4
TRACHEITIS	0	-	-	1
MILD	0	-	-	1
LUNGS				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	2	-	-	3

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 25 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		10	10	10	10
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
LUNGS (CONTINUED)					
ALVEOLAR HISTIOCYTOSIS		3	-	-	2
MINIMAL		2	-	-	2
MILD		1	-	-	0
LYMPHOID HYPERPLASIA		0	-	-	1
MILD		0	-	-	1
KIDNEYS					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
URINARY BLADDER					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		3	-	-	4
ECTASIA		0	-	-	1
MODERATE		0	-	-	1
INTRALUMINAL PROTEIN COAGULUM		2	-	-	0
PRESENT		2	-	-	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 26
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	10	10	10	10
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
HEART				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
ORAL/PHARYNGEAL				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	4
HEMORRHAGE	0	-	-	1
MARKED	0	-	-	1
STOMACH				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
LIVER				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	4	-	-	5
MONONUCLEAR CELL INFILTRATE(S)	1	-	-	0
MINIMAL	1	-	-	0
ADRENAL GL				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
SKIN				
TOTAL NUMBER EXAMINED	1	0	0	5
EXAMINED, UNREMARKABLE	1	-	-	5
SPLEEN				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
LYMPH ND, S-MAN				
TOTAL NUMBER EXAMINED	4	0	0	4

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 26 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	10	10	10	10
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
LYMPH ND, S-MAN (CONTINUED)				
CYSTIC LYMPHATIC ECTASIA	0	-	-	1
MODERATE	0	-	-	1
SINUS ERYTHROCYTOSIS	4	-	-	4
MILD	0	-	-	1
MODERATE	4	-	-	3
PLASMACYTOSIS	1	-	-	0
MODERATE	1	-	-	0
LYMPH ND, OTHER				
TOTAL NUMBER EXAMINED	1	0	0	0
SINUS ERYTHROCYTOSIS	1	-	-	-
MARKED	1	-	-	-
THYMIC REGION				
TOTAL NUMBER EXAMINED	4	0	0	0
EXAMINED, UNREMARKABLE	1	-	-	-
HEMORRHAGE	3	-	-	-
MILD	1	-	-	-
MODERATE	2	-	-	-
BRAIN				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	3	4	5	0
MENINGEAL HEMORRHAGE	0	1	0	1
MILD	0	1	0	0
MODERATE	0	0	0	1
BRAIN HEMORRHAGE	1	0	0	0
MILD	1	0	0	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 26 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	10	10	10	10
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
BRAIN (CONTINUED)				
VACUOLATION/SPONGIOSIS	1	0	0	5*
MINIMAL	1	0	0	0
MILD	0	0	0	5
SPINAL CORD				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	4	5	0
EPIDERMAL INCLUSION CYST	0	1	0	0
PRESENT	0	1	0	0
VACUOLATION/SPONGIOSIS	0	0	0	5**
MILD	0	0	0	1
MODERATE	0	0	0	3
MARKED	0	0	0	1
NERVE, SCIATIC				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
EYE				
TOTAL NUMBER EXAMINED	0	0	0	1
RETROORBITAL HEMORRHAGE	-	-	-	1
MILD	-	-	-	1
HARDERIAN GL				
TOTAL NUMBER EXAMINED	0	0	0	1
FIBROSIS	-	-	-	1
MILD	-	-	-	1
OVARIES				
TOTAL NUMBER EXAMINED	0	0	0	1
EXAMINED, UNREMARKABLE	-	-	-	1
NASAL CAVITY				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	3

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

* Significantly different from control group (p < .05)

** Significantly different from control group (p < .01)

TABLE 26 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	10	10	10	10
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
NASAL CAVITY (CONTINUED)				
HEMORRHAGE	0	-	-	1
MILD	0	-	-	1
RHINITIS	0	-	-	1
MILD	0	-	-	1
LARYNX				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	3	-	-	5
ASPIRATED BLOOD	1	-	-	0
MILD	1	-	-	0
LARYNGITIS	1	-	-	0
MILD	1	-	-	0
TRACHEA				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	4	-	-	5
ASPIRATED BLOOD	1	-	-	0
MILD	1	-	-	0
LUNGS				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	3	-	-	3
ALVEOLAR HISTIOCYTOSIS	1	-	-	1
MINIMAL	0	-	-	1
MILD	1	-	-	0
HEMORRHAGE	0	-	-	1
MILD	0	-	-	1

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 26 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		10	10	10	10
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
LUNGS (CONTINUED)					
INTERSTITIAL PNEUMONITIS		1	-	-	0
MINIMAL		1	-	-	0
KIDNEYS					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		4	-	-	3
MINERALIZATION		1	-	-	2
MINIMAL		1	-	-	2
URINARY BLADDER					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 27

VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
TISSUE ABBREVIATIONS USED FOR NEUROPATHOLOGY EVALUATION

[ABBREVIATION;ABBREVIATED NAME IN THE COMPUTER;COMPLETE NAME]

OLFACTORY BULB;OLFACTORY BULB	SPINAL CORD, LUM;SPINAL CORD, LUMBAR
PIRIFORM CORTEX;PIRIFORM CORTEX	SPINAL NERVE RTS;SPINAL NERVE ROOTS
FRONTAL CORTEX;FRONTAL CORTEX	DORSAL ROOT GANG;DORSAL ROOT GANGLIA
ANT COMMISSURE;ANTERIOR COMMISSURE	GASSERIAN GANG;GASSERIAN GANGLIA
SEPTAL NUCLEI;SEPTAL NUCLEI	SCIATIC NERVE;SCIATIC NERVE
CAUD NUC/PUTAMEN;CAUDATE NUCLEUS/PUTAMEN	TIBIAL NERVE;TIBIAL NERVE
GLOBUS PALLIDUS;GLOBUS PALLIDUS	PERONEAL/SURAL N;PERONEAL/SURAL NERVE
EXTERNAL CAPSULE;EXTERNAL CAPSULE	CEREBRAL CORTEX;CEREBRAL CORTEX
CORPUS CALLOSUM;CORPUS CALLOSUM	SUBCORT AREA NOS;SUBCORTICAL AREAS, NOS
FORNIX;FORNIX	CLAUSTRUM;CLAUSTRUM
OPTIC N/CHIASM;OPTIC NERVE/CHIASM	SUBICULUM;SUBICULUM
INTERNAL CAPSULE;INTERNAL CAPSULE	FIMBRIA;FIMBRIA
THALAMUS;THALAMUS	HIPPOCAMPUS, CA1;HIPPOCAMPUS, CA1
HYPOTHALAMUS;HYPOTHALAMUS	HIPPOCAMPUS, CA2;HIPPOCAMPUS, CA2
AMYGDALA;AMYGDALA	HIPPOCAMPUS, CA3;HIPPOCAMPUS, CA3
HIPPOCAMPUS;HIPPOCAMPUS	HIPPOCAMPUS, CA4;HIPPOCAMPUS, CA4
PARIETAL CORTEX;PARIETAL CORTEX	DENTATE GYRUS;DENTATE GYRUS
TEMPORAL CORTEX;TEMPORAL CORTEX	BRAIN, NOS;BRAIN, NOS
OCCIPITAL CORTEX;OCCIPITAL CORTEX	WHITE MATTER NOS;WHITE MATTER, NOS
MENINGES;MENINGES	PYRAMIDS;PYRAMIDS
MIDBRAIN;MIDBRAIN	STRIA MEDULLARIS.;STRIA MEDULLARIS
SUBSTANTIA NIGRA;SUBSTANTIA NIGRA	LONG. FASCICULUS;LONGITUDINAL FASCICULUS
CEREBELLAR CTX;CEREBELLAR CORTEX	POST COMMISSURE;POSTERIOR COMMISSURE
CEREBELLAR W.M.;CEREBELLAR WHITE MATTER	CEREBRAL PED;CEREBRAL PEDUNCLE
CEREBELLAR NUC;CEREBELLAR NUCLEI	DENTATE NUCLEUS;DENTATE NUCLEUS
VESTIBULAR NUC;VESTIBULAR NUCLEUS	FASTIGIAL NUC;FASTIGIAL NUCLEUS
PONS;PONS	CEREBELLAR PEDS;CEREBELLAR PEDUNCLES
MEDULLA OBL;MEDULLA OBLONGATA	OLFACTORY TRACT;OLFACTORY TRACT
TRIGEMINAL TRACT ;TRIGEMINAL TRACT	PINEAL GLAND;PINEAL GLAND
SPINAL CORD, CRV,;SPINAL CORD, CERVICAL	PARAVENT ORGAN;PARAVENTRICULAR ORGAN(S)
SPINAL CORD, THR;SPINAL CORD, THORACIC	CRANIAL N, NOS;CRANIAL NERVE, NOS
	NERVE OTHER;NERVE, OTHER

TABLE 28
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
MENINGES				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
PIRIFORM CORTEX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
FRONTAL CORTEX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
PARIETAL CORTEX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
TEMPORAL CORTEX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
OCCIPITAL CORTEX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
SEPTAL NUCLEI				
TOTAL NUMBER EXAMINED	4	5	3	3
EXAMINED, UNREMARKABLE	4	5	3	3
MISSING	1	0	2	2
CAUD NUC/PUTAMEN				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
GLOBUS PALLIDUS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
AMYGDALA				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
HIPPOCAMPUS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 28 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
THALAMUS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
HYPOTHALAMUS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
MIDBRAIN				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	2
MYELINOPATHY	0	0	0	3
MINIMAL	0	0	0	2
MILD	0	0	0	1
SUBSTANTIA NIGRA				
TOTAL NUMBER EXAMINED	5	5	5	4
EXAMINED, UNREMARKABLE	5	5	5	4
MISSING	0	0	0	1
CEREBELLAR W.M.				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
ANT COMMISSURE				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
EXTERNAL CAPSULE				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
INTERNAL CAPSULE				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
CORPUS CALLOSUM				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
FORNIX				
TOTAL NUMBER EXAMINED	3	5	2	1
EXAMINED, UNREMARKABLE	3	5	2	1
MISSING	2	0	3	4

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 28 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
CEREBELLAR CTX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
CEREBELLAR NUC				
TOTAL NUMBER EXAMINED	5	5	5	4
EXAMINED, UNREMARKABLE	5	5	5	4
MISSING	0	0	0	1
VESTIBULAR NUC				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	1
MYELINOPATHY	0	0	0	4*
MINIMAL	0	0	0	1
MILD	0	0	0	3
PONS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	0
MYELINOPATHY	0	0	0	5**
MILD	0	0	0	1
MODERATE	0	0	0	4
AXONOPATHY	0	0	0	5**
MILD	0	0	0	1
MODERATE	0	0	0	4
MEDULLA OBL				
TOTAL NUMBER EXAMINED	5	4	5	5
EXAMINED, UNREMARKABLE	5	4	5	0
MISSING	0	1	0	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

* Significantly different from control group (p < .05)

** Significantly different from control group (p < .01)

TABLE 28 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
MEDULLA OBL (CONTINUED)				
MYELINOPATHY	0	0	0	5**
MODERATE	0	0	0	3
MARKED	0	0	0	2
AXONOPATHY	0	0	0	4*
MILD	0	0	0	1
MODERATE	0	0	0	3
OLFACTORY BULB				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
OPTIC N/CHIASM				
TOTAL NUMBER EXAMINED	5	3	5	5
EXAMINED, UNREMARKABLE	5	3	5	5
MISSING	0	2	0	0
TRIGEMINAL TRACT				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	3
MYELINOPATHY	0	0	0	2
MINIMAL	0	0	0	2
AXONOPATHY	0	0	0	1
MINIMAL	0	0	0	1
SPINAL CORD, CRV				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	4	5	5	0
VACUOLATION	1	0	0	0
MINIMAL	1	0	0	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

* Significantly different from control group ($p < .05$)

** Significantly different from control group ($p < .01$)

TABLE 28 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
SPINAL CORD, CRV(CONTINUED)				
MYELINOPATHY	0	0	0	5**
MODERATE	0	0	0	1
MARKED	0	0	0	4
AXONOPATHY	0	0	0	5**
MODERATE	0	0	0	5
SPINAL CORD, THR				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	4	5	5	0
VACUOLATION	1	0	0	0
MINIMAL	1	0	0	0
MYELINOPATHY	0	0	0	5**
MODERATE	0	0	0	2
MARKED	0	0	0	3
AXONOPATHY	0	0	0	5**
MODERATE	0	0	0	5
SPINAL CORD, LUM				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	4	5	5	0
VACUOLATION	1	0	0	0
MINIMAL	1	0	0	0
MYELINOPATHY	0	0	0	5**
MILD	0	0	0	3
MODERATE	0	0	0	2

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

** Significantly different from control group (p < .01)

TABLE 28 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		5	5	5	5
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
SPINAL CORD, LUM(CONTINUED)					
AXONOPATHY		0	0	0	3
MILD		0	0	0	2
MODERATE		0	0	0	1
SPINAL NERVE RTS					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
DORSAL ROOT GANG					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
GASSERIAN GANG					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		4	-	-	5
HEMORRHAGE		1	-	-	0
MILD		1	-	-	0
SCIATIC NERVE					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
TIBIAL NERVE					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
PERONEAL/SURAL N					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 29
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 12
PERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
MENINGES				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
PIRIFORM CORTEX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
FRONTAL CORTEX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
PARIETAL CORTEX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
TEMPORAL CORTEX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
OCCIPITAL CORTEX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
SEPTAL NUCLEI				
TOTAL NUMBER EXAMINED	5	4	4	5
EXAMINED, UNREMARKABLE	5	4	4	5
MISSING	0	1	1	0
CAUD NUC/PUTAMEN				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
GLOBUS PALLIDUS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
AMYGDALA				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
HIPPOCAMPUS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 29 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 12
PERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
THALAMUS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
HYPOTHALAMUS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
MIDBRAIN				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	2
MYELINOPATHY	0	0	0	3
MINIMAL	0	0	0	3
SUBSTANTIA NIGRA				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
CEREBELLAR W.M.				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
ANT COMMISSURE				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
EXTERNAL CAPSULE				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
INTERNAL CAPSULE				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
CORPUS CALLOSUM				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
FORNIX				
TOTAL NUMBER EXAMINED	3	3	2	4
EXAMINED, UNREMARKABLE	3	3	2	4
MISSING	2	2	3	1

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 29 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 12
PERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
CEREBELLAR CTX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
CEREBELLAR NUC				
TOTAL NUMBER EXAMINED	5	3	5	5
EXAMINED, UNREMARKABLE	5	3	5	5
MISSING	0	2	0	0
VESTIBULAR NUC				
TOTAL NUMBER EXAMINED	5	4	5	5
EXAMINED, UNREMARKABLE	5	4	5	0
MISSING	0	1	0	0
MYELINOPATHY	0	0	0	5**
MINIMAL	0	0	0	1
MILD	0	0	0	3
MODERATE	0	0	0	1
AXONOPATHY	0	0	0	3
MILD	0	0	0	3
PONS				
TOTAL NUMBER EXAMINED	5	4	5	5
EXAMINED, UNREMARKABLE	5	4	5	0
MISSING	0	1	0	0
MYELINOPATHY	0	0	0	5**
MODERATE	0	0	0	5
AXONOPATHY	0	0	0	5**
MILD	0	0	0	2
MODERATE	0	0	0	3
MEDULLA OBL				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

** Significantly different from control group (p < .01)

TABLE 29 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 12
PERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
MEDULLA OBL (CONTINUED)				
MYELINOPATHY	0	0	0	5**
MODERATE	0	0	0	5
AXONOPATHY	0	0	0	5**
MODERATE	0	0	0	5
OLFACTORY BULB				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
OPTIC N/CHIASM				
TOTAL NUMBER EXAMINED	5	5	5	3
EXAMINED, UNREMARKABLE	5	5	5	3
MISSING	0	0	0	2
TRIGEMINAL TRACT				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	2
MYELINOPATHY	0	0	0	3
MINIMAL	0	0	0	3
SPINAL CORD, CRV				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	0
MYELINOPATHY	0	0	0	5**
MODERATE	0	0	0	1
MARKED	0	0	0	4
AXONOPATHY	0	0	0	5**
MODERATE	0	0	0	5
SPINAL CORD, THR				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

** Significantly different from control group (p < .01)

TABLE 29 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 12
PERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
SPINAL CORD, THR(CONTINUED)				
MYELINOPATHY	0	0	0	5**
MARKED	0	0	0	5
AXONOPATHY	0	0	0	5**
MODERATE	0	0	0	5
SPINAL CORD, LUM				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	0
MYELINOPATHY	0	0	0	5**
MILD	0	0	0	4
MODERATE	0	0	0	1
AXONOPATHY	0	0	0	2
MILD	0	0	0	1
MODERATE	0	0	0	1
SPINAL NERVE RTS				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
DORSAL ROOT GANG				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
GASSERIAN GANG				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
SCIATIC NERVE				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
TIBIAL NERVE				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
PERONEAL/SURAL N				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

** Significantly different from control group (p < .01)

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats
--

QUALITY ASSURANCE UNIT INSPECTION SUMMARY

<u>Inspection Date(s)</u>	<u>Inspection Type</u>	<u>Date QAU Report Issued To</u>	
		<u>Study Director</u>	<u>Management</u>
02-12-94	PROTOCOL	02-14-94	02-17-94
02-16-94	EVENT-ANIMAL RECEIPT	02-16-94	02-16-94
03-02-94	EVENT-EXPOSURE	03-02-94	03-15-94
03-04-94	PROTOCOL AMENDMENT #1	03-04-94	03-07-94
03-09-94	EVENT-FOBS	03-09-94	03-10-94
03-10-94	EVENT-PERFUSION	03-10-94	03-15-94
07-18-94	PROTOCOL AMENDMENT #2	07-21-94	07-21-94
11-15-94 to 11-18-94	ANATOMIC PATHOLOGY DATA, REPORT	11-30-94	02-10-95
11-18-94 to 11-22-94	ANALYTICAL CHEMISTRY DATA, REPORT	11-30-94	02-10-95
11-18-94	CLINICAL PATHOLOGY DATA, REPORT	11-30-94	02-10-95
11-22-94 to 11-30-94	RAW DATA, REPORT	11-30-94	02-10-95
02-10-95	ARCHIVES	02-10-95	02-10-95


 Craig A. Ferry, A.A.S.

Representative, Quality Assurance Unit

2-10-95

Date

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats
Chamber Atmosphere Report
(29 Pages)

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SUMMARY

The concentration of vinyl pivalate vapor in the exposure chamber atmospheres was monitored throughout the 10 days of exposure by flame ionization gas chromatography. The concentration in each exposure chamber atmosphere was determined approximately 10 times during each 6-hour exposure. The overall mean (\pm standard deviation) chamber atmosphere concentrations were 103 (\pm 1.3), 497 (\pm 6.5), and 993 (\pm 18.3) ppm, for target concentrations of 100, 500, and 1000 ppm, respectively. Vinyl pivalate was not detected in the control chamber atmosphere.

A test substance sample was drawn before and after the exposure regimen and remained 99.95% pure.

MATERIALS AND METHODS

Test Substance

One 5-gallon container of vinyl pivalate (CAS No. 3377-92-2, Lot No. JGT-3B, BRRC Sample No. 57-036) was received from Union Carbide Corporation (South Charleston, WV) on February 15, 1994. The chemical and physical properties of the test substance are described in Table 1. The compositional analyses were provided by the GLP Analytical Skill Center at the Union Carbide Corporation, South Charleston, WV, Technical Center. A summary of this report is presented in Table 2; the entire report is presented as Attachment 1. The test substance samples were drawn before and after the exposure regimen; compositional analyses indicated that the test substance was 99.95% pure and had remained stable for the duration of the exposure regimen.

Analytical Instrumentation

A Perkin-Elmer Sigma 2000 gas chromatograph (GC) equipped with a flame ionization detector was used to analyze the vinyl pivalate exposure chamber atmospheres. The GC operating conditions are presented in Table 3. A Spectra-Physics Chrom Jet Integrator provided a record of the chromatograms and chromatographic analyses as well as peak integration. The data were captured using an IBM PS/2 Computer with Spectra-Physics Chromstation/2 software. In-house software was used to compute daily statistics and also to provide an alarm system which monitored chamber concentrations.

Calibration

Calibration of the gas chromatograph was achieved by injecting gas standards, which were prepared by syringe injection of vinyl pivalate into Tedlar[®] gas bags containing air. These standards were prepared using the mathematical relationship:

$$V = \frac{C \times V_h \times MW \times 298 \times P \times 10^{-6}}{d \times 24.45 \times T \times 760}$$

where: V = required volume of calibration liquid in milliliters at temperature T (degrees K)

C = desired calibration concentration, in ppm

V_h = volume of container, in liters
 MW = molecular weight of the calibration liquid
 P = barometric pressure, in millimeters of mercury
 d = density of the calibration liquid in grams per milliliter at temperature T
24.45 = molecular volume at 298 degrees K and 760 millimeters of mercury, in liters
 T = temperature, in degrees Kelvin

The calibration curve (Figure 1) was constructed by plotting peak areas versus the gas standard concentrations. The calibration was checked at least once each week during the exposure regimen.

RESULTS AND DISCUSSION

Chamber Atmosphere Analysis

Each chamber atmosphere was analyzed for vinyl pivalate approximately twice each hour during each 6-hour exposure by flame ionization gas chromatography. The daily mean analytical concentrations are listed in Tables 4 through 7. The means of daily mean chamber atmosphere concentrations (\pm standard deviation) were 103 (\pm 1.3), 497 (\pm 6.5), and 993 (\pm 18.3) ppm, for the target concentrations of 100, 500, and 1000 ppm, respectively. No vinyl pivalate was detected in the control chamber atmosphere during the study. The estimated minimum detection limit was 4 ppm.

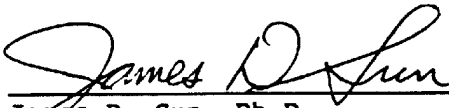
Analytical/Nominal Concentration Ratio

The daily analytical/nominal (A/NOM) vinyl pivalate concentration ratios are given in Tables 5 through 7. The nominal concentration is an estimated concentration calculated from the quantity of test substance delivered and the chamber airflow rate. The overall mean A/NOM concentration ratios were 0.94, 0.93, and 0.94, for vinyl pivalate target concentrations of 100, 500, and 1000 ppm, respectively.

Temperature and Relative Humidity

The daily mean temperature and relative humidity values for the exposure chamber atmospheres are also presented in Tables 4 through 7. The means of daily mean temperature values were 22, 23, 22, and 21°C, for the 0, 100, 500, and 1000 ppm exposure target concentrations, respectively. The means of daily mean relative humidity values were 54, 53, 45, and 47%, for the 0, 100, 500, and 1000 ppm exposure target concentrations, respectively.

Analytical Chemist:


James D. Sun, Ph.D.

2-10-95
Date

TABLE 1
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

CHEMICAL AND PHYSICAL PROPERTIES¹

Product Name:	Vynate TM Neo-5 monomer
Synonyms:	Vinyl 2,2-dimethyl-propanoate; propanoic acid; 2,2-dimethyl-ethenyl ester
Molecular Weight:	128.171
Molecular Formula:	C ₇ H ₁₂ O ₂
Vapor Density (air = 1)	4.3
Appearance and Odor:	Transparent, colorless liquid; fruit odor
Boiling Point, 760 mm Hg:	112.1°C
Solubility in Water:	Approx. 0.08% @ 20°C
Evaporation Rate (butyl acetate = 1):	2.23
Vapor Pressure at 20°C:	18.1 mm Hg
% Volatiles by weight:	100
Specific Gravity (H ₂ O = 1):	0.8725 at 20°C
Flash Point (Closed Cup):	14°C

¹Material Safety Data Sheet, Union Carbide Corporation, 03/29/93, F Number: C0134E.

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

TEST SUBSTANCE ANALYSIS¹

Component	Prestudy Area %	Poststudy Area %
Vinyl acetate	0.02	0.02
Vinyl pivalate	99.95	99.95
Vinyl 2-methylbutyrate	0.02	0.02
All other impurities	0.01	0.01

¹ The capillary gas chromatographic compositional analyses were provided by the GLP Analytical Skill Center at the Union Carbide Corporation, South Charleston, WV, Technical Center. In addition, gas chromatography-mass spectrometry and nuclear magnetic resonance spectroscopy were independently used to confirm the sample's identity.

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

GAS CHROMATOGRAPH OPERATING PARAMETERS

Chromatograph:	Perkin-Elmer Sigma 2000
Detector:	Flame Ionization
Column:	SPB-1, 1 μ M, 30 m x 0.75 mm glass capillary
Column temperature:	120°C
Injector temperature:	60°C gas sample valve
Detector temperature:	250°C
Carrier	4.5 mL/minute Nitrogen
Sample size:	0.1 cc
Retention time:	3.0 minutes
GC attenuation:	Range = 10
Minimum detection limit:	approx. 4 ppm
Integrator attenuation:	512

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

CHAMBER ATMOSPHERE DATA: 0 PPM (CONTROL) CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)
1	20.3	50.4	<MDL
2	20.9	54.7	<MDL
3	21.2	56.1	<MDL
4	21.8	55.8	<MDL
5	21.7	49.8	<MDL
6	22.4	50.8	<MDL
7	22.7	55.2	<MDL
8	22.5	63.1	<MDL
9	20.8	51.0	<MDL
10	21.3	48.8	<MDL
Mean:	21.6	53.6	<MDL
SD:	0.80	4.31	—

TEMP = temperature (daily mean)

RH = relative humidity (daily mean)

A = analytical concentration (daily mean)

SD = standard deviation

<MDL = less than the estimated minimum detection limit

TABLE 5
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

CHAMBER ATMOSPHERE DATA: 100 PPM CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)	±SD	NOM (ppm)	A/NOM
1	22.2	51.1	104	1.2	109	0.95
2	22.6	53.6	101	0.9	109	0.93
3	21.8	54.0	102	0.9	109	0.94
4	23.2	51.5	104	1.3	109	0.95
5	23.4	48.8	102	0.8	109	0.94
6	23.2	49.1	104	1.0	106	0.98
7	23.6	53.4	101	0.8	109	0.93
8	22.5	64.0	103	1.0	106	0.97
9	21.4	51.1	104	1.0	114	0.91
10	22.0	49.5	104	1.2	109	0.95
Mean:	22.6	52.6	103	---	109	0.94
SD:	0.74	4.42	1.3	---	2.2	0.020

TEMP = temperature (daily mean)
 RH = relative humidity (daily mean)
 A = analytical concentration (daily mean)
 SD = standard deviation
 NOM = nominal concentration
 A/NOM = analytical concentration/nominal concentration

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

CHAMBER ATMOSPHERE DATA: 500 PPM CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)	±SD	NOM (ppm)	A/NOM
1	21.2	. a	497	9.8	535	0.93
2	20.7	a	495	7.8	527	0.94
3	22.5	37.4	487	3.2	530	0.92
4	22.4	42.8	494	4.1	532	0.93
5	21.6	42.7	489	4.7	543	0.90
6	21.8	44.8	497	7.9	532	0.93
7	22.4	49.7	500	8.7	532	0.94
8	23.7	50.5	501	6.0	532	0.94
9	22.6	47.8	507	5.2	535	0.95
10	22.7	46.4	506	5.3	535	0.95
Mean:	22.2	45.3	497	---	533	0.93
SD:	0.86	4.30	6.5	---	4.2	0.015

^aA notation was made that the gauge was not functioning properly on this date.

TEMP = temperature (daily mean)

RH = relative humidity (daily mean)

A = analytical concentration (daily mean)

SD = standard deviation

NOM = nominal concentration

A/NOM = analytical concentration/nominal concentration

TABLE 7
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

CHAMBER ATMOSPHERE DATA: 1000 PPM CHAMBER

Exposure Day	TEMP (°C)	RH (%)	A (ppm)	±SD	NOM (ppm)	A/NOM
1	21.0	38.7	993	8.6	1073	0.93
2	20.0	42.9	1018	6.8	1073	0.95
3	20.8	41.4	977	8.7	1062	0.92
4	21.5	49.8	961	2.8	1043	0.92
5	21.7	42.6	980	6.3	1046	0.94
6	21.7	43.6	1000	6.6	1062	0.94
7	22.4	54.8	996	11.3	1057	0.94
8	21.4	55.8	981	10.7	1049	0.94
9	21.4	50.6	1007	8.7	1054	0.96
10	21.5	50.2	1016	5.5	1065	0.95
Mean:	21.3	47.0	993	—	1058	0.94
SD:	0.64	5.94	18.3	—	10.5	0.013

TEMP = temperature (daily mean)

RH = relative humidity (daily mean)

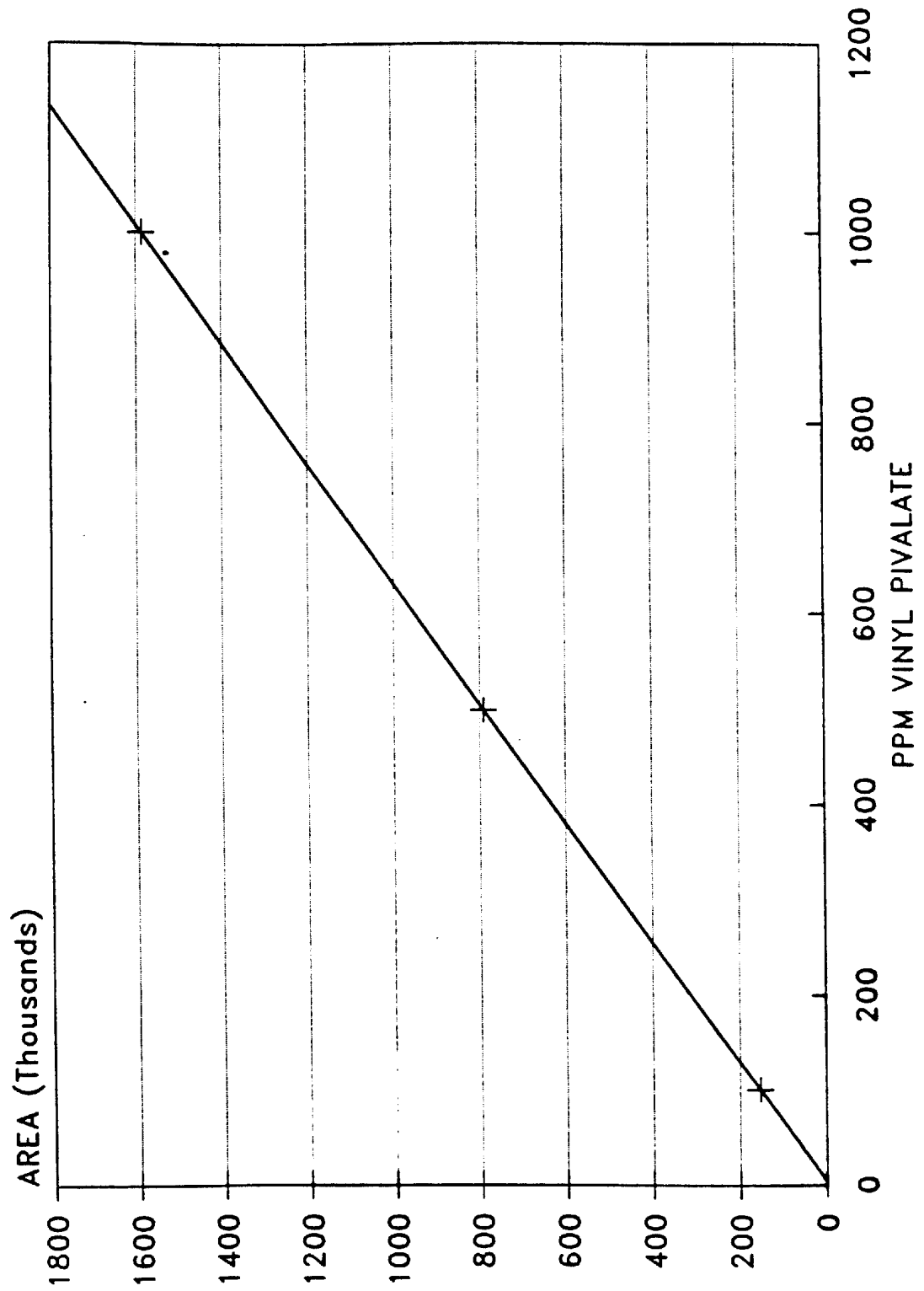
A = analytical concentration (daily mean)

SD = standard deviation

NOM = nominal concentration

A/NOM = analytical concentration/nominal concentration

FIGURE 1. VINYL PIVALATE CALIBRATION



Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats
Test Substance Characterization Report



Union Carbide Corporation

STUDY TITLE

GLP Analysis-Final Report

TEST SUBSTANCE

VYNATE™ Neo-5 Monomer
Vinyl Pivalate

DATA REQUIREMENT

U.S. FDA, 21 CFR 58
U.S. EPA TSCA, 40 CFR 792
U.S. EPA FIFRA 40 CFR 160

STUDY DIRECTOR

Alexander E. Gabany, Jr.

STUDY COMPLETED ON

March 30, 1994

PERFORMING LABORATORY

Union Carbide Corporation
PO Box 8361
South Charleston, West Virginia 25303

UCC R/D LABORATORY PROJECT ID

Study # 37-AEG-133

SPONSOR COMPANY

Union Carbide Corporation
39 Old Ridgebury Road
Danbury, Conn. 06817-0001

STUDY COMPLIANCE STATEMENT

Study Compliance Statement for Union Carbide Corporation (UCC) Study # 37-AEG-133,
VYNATE™ Neo-5 Monomer (vinyl pivalate) study for Bushy Research Center.

In accordance with UCC's intent that all tests conducted by our facility follow good laboratory practices, UCC's study director for the above test confirms that the study was conducted in compliance with Good Laboratory Practice standards: TSCA, 40 CFR 792; FIFRA, 40 CFR 160 and FDA, 21 CFR 58. All original raw data, records, protocols, samples and final reports are being retained at UCC's South Charleston, WV, Technical Center.



Alexander E. Gabany, Jr.
Study Director

3/21/94
Date

PROTOCOL DEVIATION STATEMENT

Protocol Deviation Statement for Union Carbide Corporation (UCC) Study # 37-AEG-133, VYNATE™ Neo-5 Monomer (vinyl pivalate) study for Bushy Run Research Center.

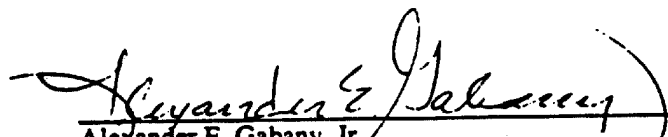
In accordance with UCC's intent that all tests conducted by our facility follow good laboratory practices, UCC's study director for the above test confirms that there were no protocol deviations taken during the study. The study was conducted in compliance with the protocol established and signed on 2/21/94 by Alexander E. Gabany, GLP Study Director.



Alexander E. Gabany, Jr. 3/31/94
Study Director date

SIGNATURE PAGE

Submitted by: Union Carbide Corporation
P.O. Box 8361
South Charleston, West Virginia 25303

Prepared by:


Alexander E. Gabany, Jr.
Study Director
3/31/94
date


Richard A. McDonie
GC/MS Skill Area Specialist
4-11-94
date

Quality Assurance Review by:

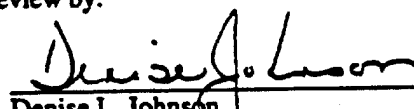

Denise L. Johnson
GLP Quality Assurance Unit
(QAU) Representative
4-15-94
date

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**VYNATE™ Neo-5 Monomer
Vinyl Pivalate**

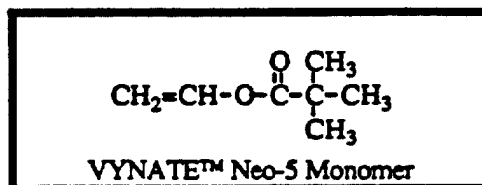
**Vinyl Pivalate
Study # 37-AEG-133**

ABSTRACT VYNATE™ Neo-5 Monomer (vinyl pivalate) was analyzed to provide analytical data as part of the toxicity study at Bushy Run Research Center. The analyses were performed in compliance with Good Laboratory Practice standards (GLP): TSCA, 40 CFR 792; FIFRA, 40 CFR 160; and FDA, 21 CFR 58. Gas chromatography-mass spectrometry (GC/MS) and nuclear magnetic resonance spectroscopy (NMR) techniques were independently used to confirm the sample's identity. Purity, measured by capillary GC, is ~99.9% for both the pre-study and the post-study sample. The samples were received from Bushy Run Research Center. All raw data, documentation, records, protocols, samples and final reports are being retained.

INTRODUCTION Richard C. Wise, this study's sponsor, requested that the Bushy Run Research Center (BRRC) test VYNATE™ Neo-5 Monomer (vinyl pivalate) for toxicity. Such studies must follow GLP standards established by the EPA that require they be conducted with authentic material whose identity and purity are verified analytically.

An ~40 gram sample of VYNATE™ Neo-5 Monomer (vinyl pivalate) (37-AEG-136) was received 2/16/94 in an amber glass bottle for analytical characterization. This sample is a subsample of a larger quantity of vinyl pivalate (Lot # JGT-3B, BRRC# 57-036) tested at Bushy Run Research Center. A GLP protocol describing the analytical characterization of the sample was prepared (Appendix 1). The protocol called for structural identification by NMR and GC/MS and for the capillary GC measurement of any impurities identified by GC/MS. The post-study sample (37-AEG-136R) was received on 3/15/94.

Shown at right is the structure of VYNATE™ Neo-5 Monomer (vinyl pivalate); its Chemical Abstracts Service Registry number (CAS #) is 3377-92-2.



DISCUSSION The data from the analyses are summarized below.

NMR Analyses Proton and carbon NMR data were collected in the UCC NMR Skill Center using a General Electric GN-300NB spectrometer. The acquisition parameters are shown in the figures; for the ¹H NMR spectrum, the pulses used correspond to <3° flip angles; the ¹³C flip angles were 30°; the ¹³C{¹H} (proton decoupled ¹³C) spectrum used Waltz 16 modulation for ¹H decoupling. The spectra were not acquired under quantitative conditions; the acquisition conditions were established to identify the major component and to look for any substantial impurities. The sample was dissolved in deuteriochloroform for analysis; tetramethylsilane (TMS) was added to provide an internal chemical shift reference. The TMS and deuteriochloroform were used as received.

Figure 1 shows the ¹H NMR spectrum obtained from the sample 37-AEG-136. The observed chemical shifts, spin-spin coupling patterns, and relative intensities are appropriate for vinyl pivalate. The CH of the vinyl group gives the four lines (doublet of doublets) at 7.3 to 7.2 ppm; the doublet of doublets at 4.9 to 4.8 ppm arises from the vinyl CH₂ proton *cis* to the oxygen; the doublet of doublets at 4.6 to 4.5 ppm arises from the other proton of the CH₂, *trans* to the oxygen. The three equivalent methyls in the t-butyl group gives rise to the single resonance at 1.24 ppm. The small peaks symmetrically arranged about the base of the t-butyl methyl resonance are the expected ¹³C satellites of the methyl peak. The remaining lines, 1.33 and 1.42 ppm, are probably spinning side bands of the strong resonance. The line at 0.0 ppm is the TMS, which is the chemical shift reference. No impurities are evident in this spectrum.

Figure 2 shows the ¹³C{¹H} spectrum for the same sample. No unusual or unexpected resonances are seen. The observed five resonances are appropriate for vinyl pivalate: the carbonyl carbon at 175.1 ppm, the vinyl CH at 141.7 ppm, the vinyl CH₂ at 97.1 ppm, the quaternary t-butyl carbon at 38.6 ppm, and the t-butyl methyls at 26.9 ppm. The triplet at 77.3 ppm is the deuteriochloroform solvent, and the singlet at 0.0 ppm is the TMS, which is the chemical shift reference. The NMR spectra are totally consistent with the sample being vinyl pivalate which contains no major organic impurities.

GC/MS Analysis Electron ionization (EI) mass spectral data was collected in the UCC MS Skill Center using a Finnigan TSQ-70 mass spectrometer interfaced to a Hewlett-Packard (HP) 5890 gas chromatograph. The sample, 37-AEG-136, was analyzed by injecting 0.1 μ L aliquots onto a CP-Sil-5-CB capillary column held at 30°C for 4 minutes, and then programmed to 250°C at 8°/minute. Figure 3 shows the EI total ion current chromatogram for the sample (scanned from m/z 10 to m/z 310 EI mode). This chromatogram is annotated with identifications based on the components' EI spectrum.

Capillary GC A HP 5890 gas chromatograph equipped with a flame ionization detector was used to analyze samples 37-AEG-136 and 37-AEG-136R. Aliquots (1 μ L) were injected via autoinjector with a 100:1 split ratio onto a DB-1 capillary column started at 60°C and held for 4 minutes then programmed to 250°C at 12°/minute and held for 5 minutes (see Figure 4). The averages of triplicate analysis are given below (normalized chromatogram area percent).

<u>Component name</u>	<u>37-AEG-136</u>	<u>37-AEG-136R</u>
vinyl acetate	0.02	0.02
vinyl pivalate	99.95	99.95
vinyl 2-methylbutyrate	0.02	0.02
all other impurities	0.01	0.01

CONCLUSION NMR spectral data and mass spectral fragmentation data from the UCC Skill Centers show that this sample is VYNATE™ Neo-5 Monomer (vinyl pivalate). These independent methods satisfy the analytical requirements for structural identification, as defined in the sample protocol. Sample purity, measured by capillary GC, is = 99.9% for both the pre-study and post-study sample.

ARCHIVES All raw data, records, protocols, samples and final reports are being retained at UCC's South Charleston, WV, Technical Center as follows:

- raw data from GC, NMR, and GC/MS studies are in 770-361, 770-127, and 770-123, respectively;
- protocols, notebook, and other records are to be kept in the GLP archives;
- the remainder of each sample is being kept in a locked GLP sample box in 770-361.

ACKNOWLEDGEMENTS We would like to thank Trudy Barker for sample handling, collecting the GC data, and preparing the bulk of the report, and Kathy Canterbury for collecting the NMR data.

NOTEBOOK REFERENCE: 37-AEG-133 and related pages

Confidentiality No claim of confidentiality is made for any information contained in this study as it pertains to use by any government agency to which it is submitted. This document, however, is proprietary to UCC and is confidential and trade secret information in all other countries and for all purposes other than those directly related to the purposes of the reviewing agency. Information contained in these studies should not be reviewed, abstracted or used by persons other than the agency without the expressed written consent of UCC except as required to carry out statutory requirements.

¹H NMR spectrum of 1,2,3,4-tetrahydro-2H-pyran-2-one. The spectrum shows peaks at 1.238, 1.024, 1.449, 1.425, 1.332, 4.547, 4.542, 4.528, 4.888, 4.883, 4.898, 4.893, 7.237, 7.258, 7.264, and 7.304 ppm. Integration values are shown below the peaks: 1.000, 1.024, 1.449, 1.425, 1.332, 4.888, 4.883, 4.898, 4.893, 7.237, 7.258, 7.264, and 7.304. An inset shows a zoomed-in view of the aromatic region with peaks at 7.237, 7.258, 7.264, and 7.304 ppm.

RECEIVED
Kathleen Connelley 2/1/94
SPT 111508
Arnold M. Levine 3/2/94

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REC101  .C01
RC 11000 01500000
37AC136 71N1L PIVATL
M03742 COC 37100  M 5001

ONE PL. SE. SEQUENCE

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D5      =      1.00 SEC
MA      =      120
3712C   =      32700
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EM       =      10
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005 L1 P/W = 0
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TO        -1.00 PW/PW

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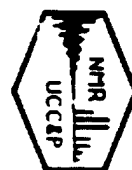
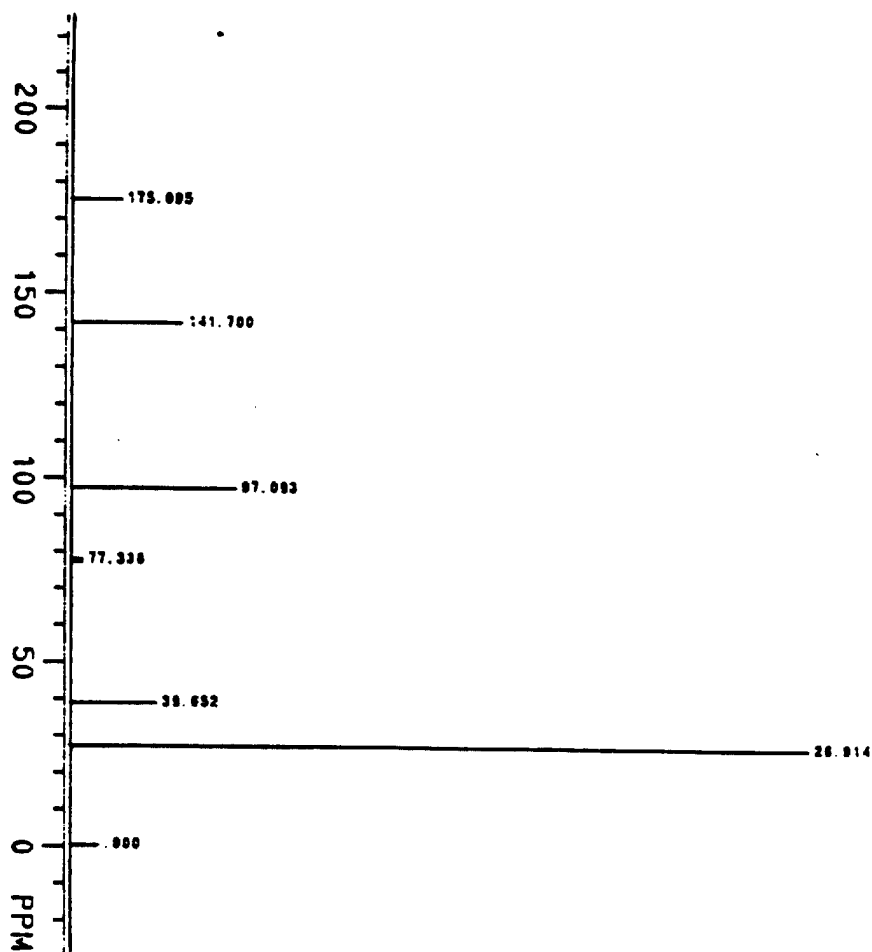


Figure 2 — ^{13}C NMR Spectrum of 37-AEG-136 [VYNATE™ Neo-5 Monomer (vinyl pivalate)]



TECHNICIAN
Wendy G. Gribble
David M. Swiney 3/2/94
3/2/1994

AC1302 C01
EC CH200 02MAR94
37AEG136 VINYL PIVALATE 13C
M03242 CDCL3/TMS SING
ONE PUL SEQUENCE
P2 = 4.02 UFG
B3 = 3.00 SEC
M1 = 120
B17E = 63336
ADC = 12
A1 = 10
F1 = 50
F2 = 10.7
F3 = 6.3
F4 = 7.24
LOCK = 1000.32
SW = 4/-10000.0 HZ
DE/DW = 50 UFG
A1 = 1.00 SEC
W = 75.310000
F2 = 300.3100000
DOS H1 PUL = 00
DOS L0 PUL = 70
DEC PUL = 72
DEC SDRIVE = 3
SCALE = 1000.00 HZ/CM
13 2324 PPM/CM
FROM -328.13
TO -40.50 PPM



Figure 3 — Capillary GC/MS RIC of 37-AEG-136 [VYNATE™ Neo-5 Monomer (vinyl pivalate)]

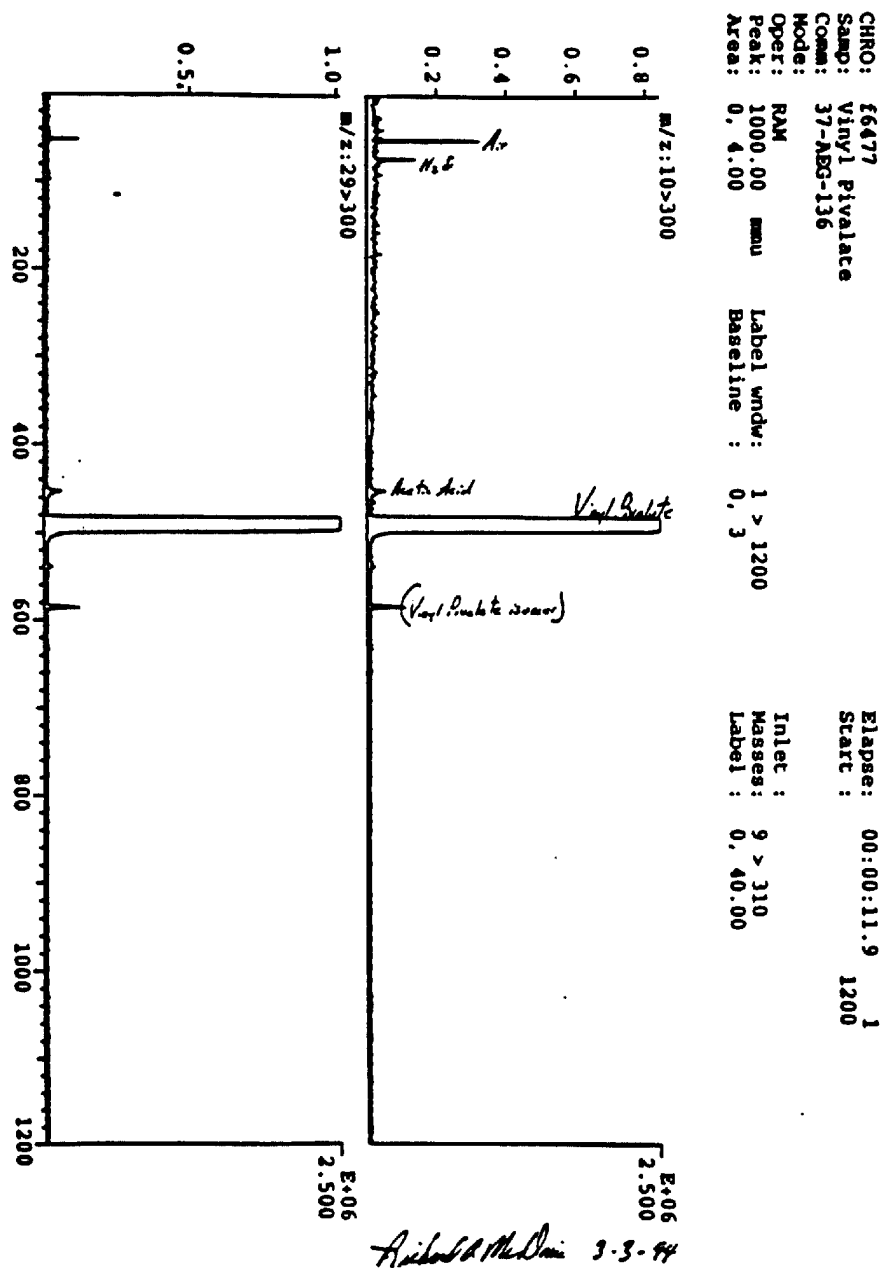


Figure 4 — Capillary Gas Chromatogram of 37-AEG-136 [VYNATE™ Neo-5 Monomer (vinyl pivalate)]

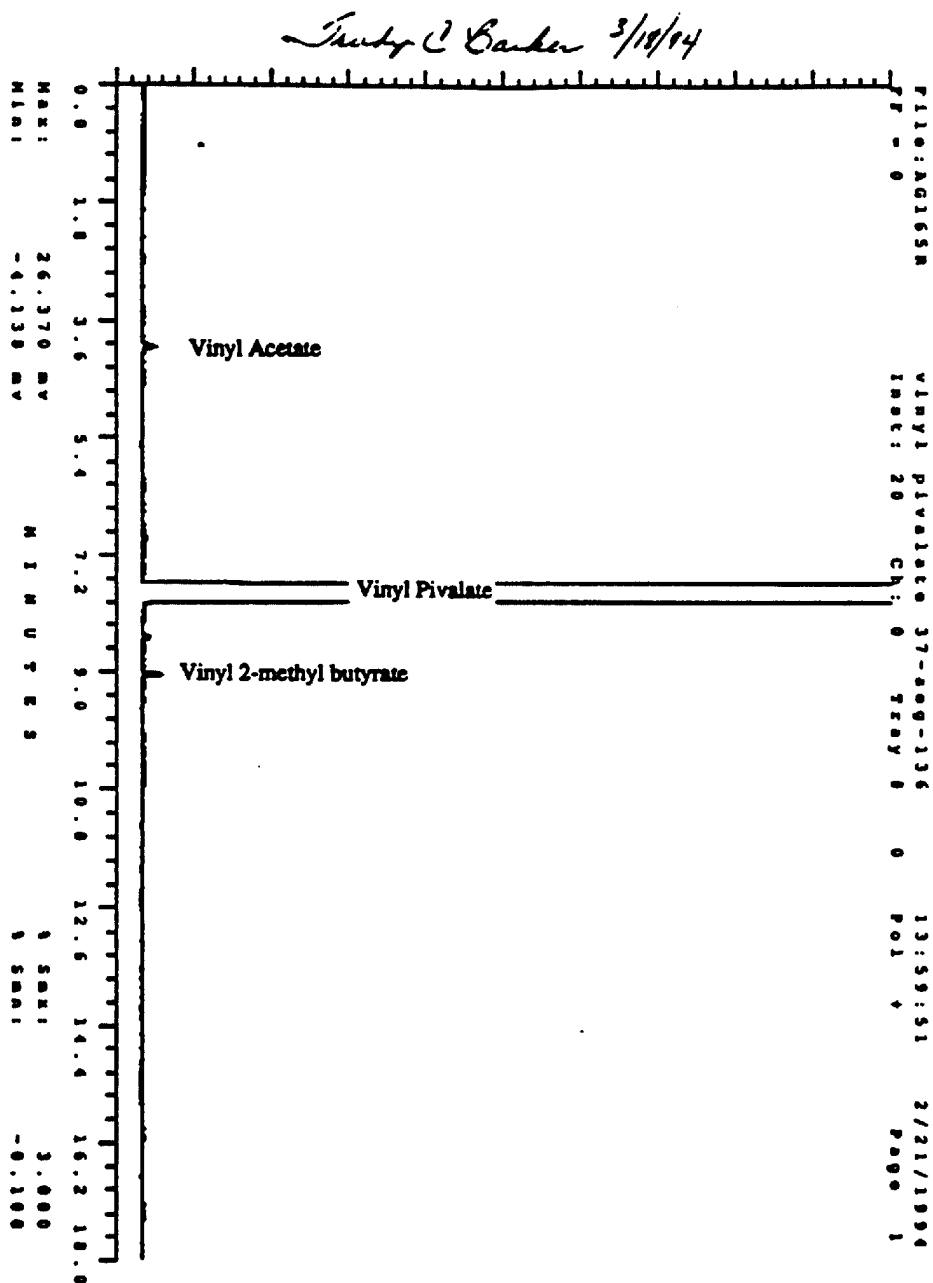
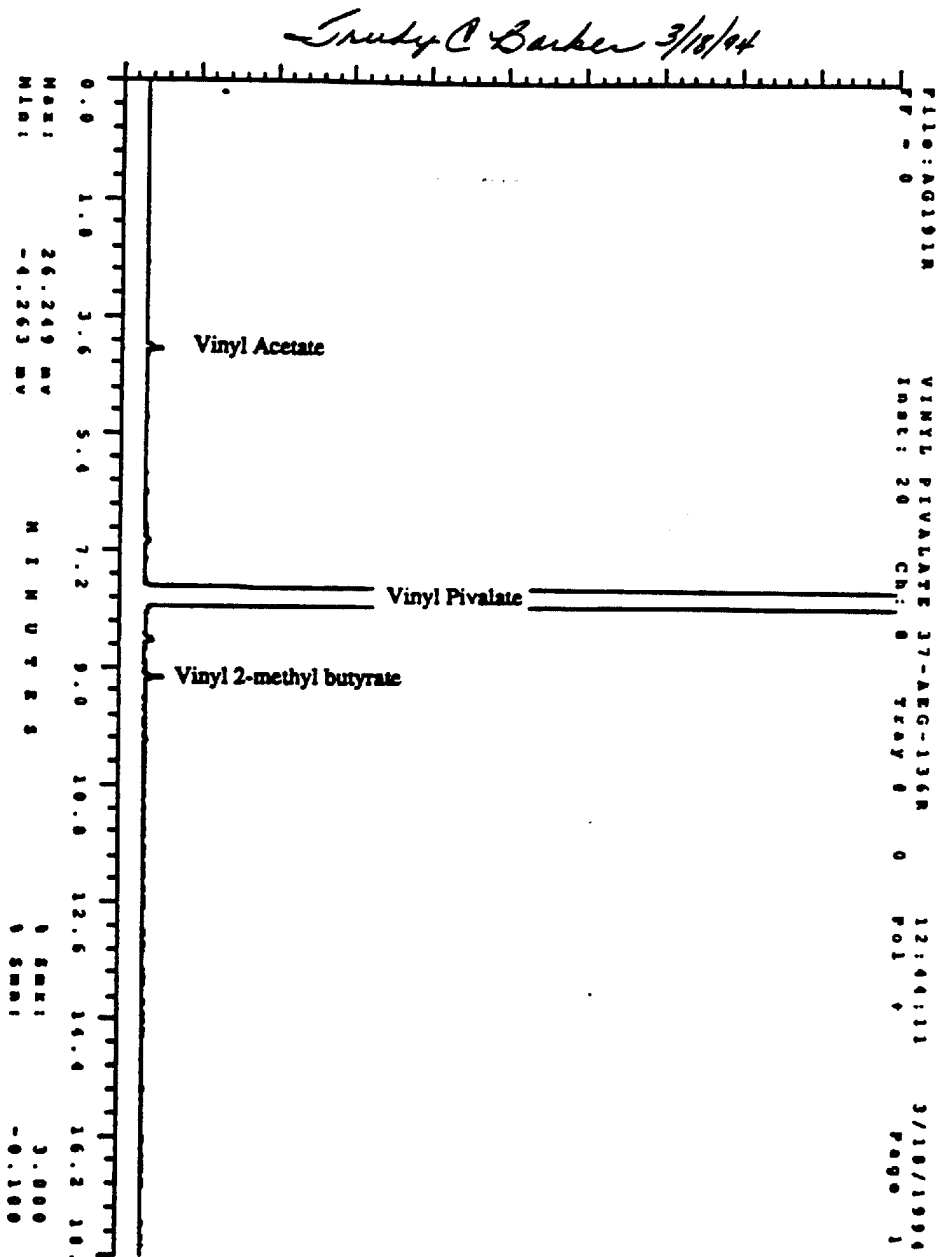


Figure 5.- Capillary Gas chromatogram of 37-AEG-136R [VYNATE™ Neo-5 Monomer (vinyl pivalate)]



Study # 37-AEG-133

page 14 of 16

APPENDIX I

Protocol

PROTOCOL

GOOD LABORATORY PRACTICE (GLP) STUDY

title

VYNATE™ NEO-5 MONOMER

purpose

Analytical Characterization of Sample(s) for
Ten Day Inhalation Studies at Bushy Run Research Center (BRRC)

study number

37-AEG-133

sponsor

SOLVENTS AND COATING MATERIALS DIVISION (SCMD)
Union Carbide Corporation (UCC)
39 Old Ridgebury Road, Danbury, Conn. 06817-0001

testing facility

UCC Technical Center,
South Charleston, WV 25303 (Location 511)

Proposed Starting Date:

Monday, February 21, 1994

Proposed Completion Date:

April 1, 1994

Estimated Date of Final Report:

May 1, 1994

Test Substance(s) 37-AEG-18

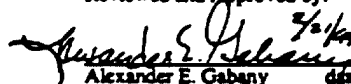

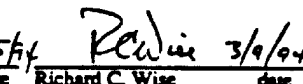
Name	VYNATE™ NEO-5 Monomer
Source	Lot # JGT-3B; UCC, South Charleston, WV
CAS Registry No.	3377-92-2
Description	Transparent colorless liquid, fruit odor
Purity	~99% vinyl pivalate; 9-13 ppm monomethyl ether of hydroquinone inhibitor, <1% vinyl acetate
Health/Safety	moderately toxic; stable. MSDS available upon request
Storage Conditions	Refrigerate

Study Design

The test substance(s) will be characterized by:

- Verification of identity by proton- and carbon-NMR.
- Verification of identity by GC/MS. An attempt will be made to identify all impurities at the concentration of ≥0.1 wt. %.
- Quantitation of the identified impurities by capillary GC.

Reviewed and Approved by:

		
Alexander E. Gabany	Denise L. Johnson	Richard C. Wise
GLP Study Director	GLP Quality-Assurance Unit (QAU) Representative	Manager of Product Safety, SCMD, Sponsor

This study will be performed in compliance with the following GLP standards: FDA, 21 CFR, Part 58; TSCA, 40 CFR, Part 792; and FIFRA, 40 CFR, Part 160. All changes of an approved protocol and the reasons therefor shall be documented, signed by the study director, dated, and maintained with the protocol. All raw data, reports and a sample of test substance from this study will be retained at Location 511 for at least 10 years after completion of the study. A comprehensive final report will be submitted to the Sponsor within one month after the completion of the analysis. The final report will be inspected by the QAU and will contain a signed quality assurance statement.

QAU STATEMENT

Quality Assurance Unit Study Inspection Summary

Test Substance: VYNATE™ NEO-5 MONOMER (VINYL PIVALATE)

Study No.: 37-AEG-133

Study Director: A.E. Gabany, B.S.

The Quality Assurance Unit of the Union Carbide Technical Center conducted the inspections listed below and reported the results to the study director and management on the date indicated. It is the practice of this Quality Assurance Unit to report the results to both the study director and management.

<u>Date</u>	<u>Inspection Type</u>	<u>Date QAU Report Issued</u>	
		<u>To Study Director</u>	<u>To Management</u>
Feb. 10, 1992	Laboratory Compliance Review*	Feb. 10, 1992	May, 1992
Feb. 25, 1994	Protocol Compliance Review	Feb. 25, 1994	Feb. 25, 1994
Apr. 15, 1994	Final Report Compliance Review	Apr. 15, 1994	Apr. 15, 1994

*The process of doing the GLP characterization studies is audited periodically to assure these studies comply with GLP requirements. The QA unit is exempted from performing in-life study inspections for studies designed to determine physical and chemical characteristics of a test substance as described in 40 CFR 792.135.

 4-15-94
Denise L. Johnson, QAU Representative (Date)
Good Laboratory Practices/Quality Assurance

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

Anatomic Pathology Report

(33 Pages)

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SUMMARY

Male and female Fischer 344 rats, purchased from Harlan Sprague Dawley, Inc, Indianapolis, IN, were exposed to 0 (control), 100, 500, or 1000 ppm of vinyl pivalate vapor for 6 hours/day for 5 consecutive days for the first week, and 3, 4, or 5 days the following week in order to evaluate any possible toxic effects which might result from inhalation exposure. There were 10 rats/sex/group. All animals survived to sacrifice and were euthanized at the end of the exposure period. Five rats/sex/group were perfused with fixative in preparation for a detailed microscopic examination of the nervous system on study Days 11 (males) and 12 (females). Perfused rats received an abbreviated necropsy. The remaining 5 rats/sex/group were sacrificed on study Day 13 and received a complete necropsy. Selected tissues were collected and preserved in fixative from all study animals. Microscopic examinations were performed on selected tissues for all animals, with the 5 perfused rats/sex/group receiving detailed examinations of their nervous systems.

The only gross lesions found in any animals which might be associated with chemical exposure involved the skin. Periorcular and/or perinasal crusts/scab/scale and periorcular (eyelid) swelling occurred in various exposure groups, including controls, but appeared to be generally more prevalent in the 500 and 1000 ppm concentration group animals. These lesions may indicate a mild irritant effect of chemical exposure in some animals.

Significant microscopic lesions, which were attributed to exposure to vinyl pivalate, were found in the brain and spinal cords of all the rats, both perfused and nonperfused, in the 1000 ppm group. In nonperfused animals, the lesions were described as vacuolation/spongiosis, which affected primarily the brain stem (medulla and pons) and the ventral/lateral white matter tracts of the spinal cord. Brain lesions were graded mild to moderate, and spinal cord lesions were graded mild to marked. Occasional control group animals had brain vacuolation/spongiosis, graded minimal, but the lesions in controls were located at different sites than those of chemically-exposed rats. In perfused rats, a similar lesion to vacuolation, termed myelinopathy after being confirmed with special stains, was observed consistently in the white matter of the pons, medulla oblongata, and spinal cord, and variably in the vestibular nuclei, midbrain, and trigeminal tracts of 1000 ppm group rats of both sexes. Brain lesions ranged in severity from minimal to marked at various sites. Spinal cord lesions ranged from mild to marked. In addition to myelinopathy, many animals also had minimal to moderate axonopathy at the same sites, as confirmed by Bielschowsky's stain for axons. There were no similar brain or spinal cord lesions in any rats receiving less than 1000 ppm of vinyl pivalate. There were no lesions in tissues other than the nervous system, examined for nonperfused rats, which were attributed to vinyl pivalate exposure.

INTRODUCTION

In 2 previous studies (BRRC Reports 52-133 and 93U1317), single and repeated oral gavage dosing with vinyl pivalate, respectively, produced lesions of neurotoxicity in the spinal cords and brains of rats which were interpreted as

a primary myelinopathy and/or axonopathy. This study was performed to evaluate the possible toxic effects which might result from a 10-day repeated vapor inhalation exposure to the test substance.

MATERIALS AND METHODS

Nonperfused (Immersion-fixed) Rats

Necropsy

After the tenth exposure, rats were anesthetized with halothane and were euthanized by severing their brachial vessels to permit exsanguination. All animals received a complete necropsy and the following tissues were collected and preserved in 10% neutral buffered formalin:

<u>gross lesions</u>	duodenum
<u>lungs</u> (with mainstem bronchi)	jejunum
<u>nasopharyngeal tissues</u>	ileum
<u>brain</u>	cecum
cerebral cortex	colon
cerebellar cortex	rectum
medulla/pons	mammary gland (females)
pituitary	skeletal muscle
thyroid-parathyroid complex	(gastrocnemius)
thymic region	sternum
sternum	femur (including articular surface)
salivary gland	<u>trachea</u>
pancreas	<u>heart</u>
epididymis	<u>liver</u>
prostate	<u>spleen</u>
seminal vesicles	<u>kidneys</u>
vagina	<u>adrenals</u>
uterus (corpus and cervix)	<u>testes</u>
aorta	ovaries
skin	<u>urinary bladder</u>
esophagus	<u>sciatic nerve</u>
<u>stomach</u>	eyes
	<u>spinal cord</u>
	<u>larynx</u>
	submandibular lymph nodes
	bone marrow smear
	tail (animal identification)

Lungs were inflated with fixative through the trachea.

Spinal cord sections include cervical, thoracic and lumbar regions.

The right kidney was sectioned transversely and the left was cut longitudinally.

Organ weights were collected for the following tissues from all animals:

liver	ovaries
kidneys	brain (including
adrenals	brain stem)
heart	spleen
testes	lungs

Histopathology

Microscopic examinations were performed on the above underlined tissues for all nonperfused animals from the control and high concentration groups. In addition, the brain and spinal cords were examined from those animals assigned to the mid and low concentration groups.

All tissues to be examined were paraffin embedded, sectioned at approximately 5 microns and stained with hematoxylin and eosin. Lesions were graded, when possible, into 5 categories (minimal, mild, moderate, marked, and severe).

Statistics

The frequency of histologic lesions was compared between each exposure group and the control group using the Fisher's Exact Test. The probability value of <0.05 (two-tailed) was used as the critical level of significance.

Perfused Rats - Neuropathology Evaluation

Necropsy

Following the eighth (males) or ninth (females) exposure, 5 rats/group/sex were anesthetized with an i.p. injection of a mixture of sodium pentobarbital in the form of Euthanasia-6 Solution (Veterinary Laboratories, Inc., Lenexa, KS) and heparin. When a deep plane of surgical anesthesia had been induced (as determined by the disappearance of all observable reflexes, including the toe pinch and corneal reflexes), the chest cavity was opened and a cannula placed through the apex of the heart into the left ventricular chamber. A phosphate buffered solution of 4% para-formaldehyde followed by a 5% glutaraldehyde solution was then infused through this catheter into the left ventricle using a gravity feed perfusion apparatus. When the right ventricle began to bulge outward, the lateral wall of this ventricle was incised to allow the perfusion fluid to exit. The para-formaldehyde solution was introduced first as a flush and then approximately 250 - 500 ml of the glutaraldehyde fixative was perfused through each rat.

After perfusion fixation, the animals received an abbreviated necropsy. The calvaria and the dorsal arches of the vertebrae were removed and the sciatic nerve and its branches were exposed but left in situ. The following tissues were removed and immersion fixed in a refrigerated solution of 5% glutaraldehyde:

brain	dorsal root ganglia
cerebral cortex	dorsal and ventral nerve roots
midbrain	Gasserian ganglia
cerebellar cortex	sciatic nerve
medulla/pons	tibial nerve
spinal cord	sural and peroneal nerves

The tail was saved as animal identification.

Spinal cord sections include cervical, thoracic and lumbar regions.

Tissues examined by light microscopy were stored, after trimming, in 10% neutral buffered formalin (NBF) and those tissues retained for a possible electron microscopic evaluation were stored refrigerated in a solution of 5% glutaraldehyde.

Histopathology

Microscopic examinations were performed on the above tissues for 5 animals/sex from the control and high exposure groups. The brain and spinal cord were also examined for the mid and low concentration groups.

The sections of brain, spinal cord, Gasserian ganglia, nerve roots, and dorsal root ganglia were embedded in paraffin. Five to 6 micron sections of each of these tissues were prepared and stained with hematoxylin and eosin, luxol fast blue, and the Bielschowsky's techniques. The peripheral nerves were embedded in glycol methacrylate, sectioned at 2 microns, and stained with hematoxylin and eosin, toluidine blue, and the Bielschowsky's technique.

Thirty-eight neuroanatomic locations were specifically designated, although many more (that is, all areas of every section) were examined. Microscopic findings were graded as to severity into 5 categories, where 1 = minimal, 2 = mild, 3 = moderate, 4 = marked, and 5 = severe.

Statistics

The frequency of histologic lesions was compared between each exposure group and the control group using the Fisher's Exact Test. The probability value of <0.05 (two-tailed) was used as the critical level of significance.

RESULTS AND DISCUSSION

The gross lesions found in this study are presented in Tables 1 and 3 for male rats and 2 and 4 for females. The gross findings are separated in the tables for the perfused and nonperfused animals. Gross lesions were infrequent in all tissues. The only lesions which may have been related to chemical exposure in a few animals involved the periocular and/or perinasal skin. Swollen eyelids were seen in 1 male and 3 females from the 1000 ppm group (perfused and nonperfused rats combined), as well as in 1 female/group from the control and 100 ppm groups. Crust/scab/scale of the periocular/perinasal

skin was present in 2 males/group from the control and 100 ppm groups, 4 males from the 500 ppm group, and 5 males from the 1000 ppm group. It was present in 1 female/group from the 100 and 500 ppm groups and 5 females from the 1000 ppm group. Although periocular skin lesions occurred more frequently in the high concentration group rats than in controls, the significance of the lesions is not certain. It may be the result of chemical irritation in some animals, but, as all study animals were bled from the retroorbital sinus shortly before sacrifice, eyelid irritation may also have resulted from the bleeding procedure. Eye trauma from bleeding was observed in several animals from various groups at necropsy. A few rats had meningeal hemorrhage of the brain or spinal cord, but there was no association of the lesions with chemical concentration and they are, therefore, considered to be incidental findings.

The microscopic lesions found in this study are presented in Tables 5 and 6 for nonperfused male and female rats, respectively (all tissues), and in Tables 8 and 9 for perfused male and female rats, respectively (nervous system tissue evaluations). Table 7 presents the tissue abbreviations used for the neuropathology evaluation. There were no microscopic lesions found in tissues other than the nervous system, which were attributed to vinyl pivalate exposure. One 1000 ppm group male had blepharitis and periocular skin edema which were related to eye trauma and infection, possibly from retroorbital bleeding. None of the other rats with gross periocular skin lesions had corresponding microscopic findings.

Lesions which were attributed to vinyl pivalate exposure were found in the brains and spinal cords of all male and female rats, both perfused and nonperfused, from the 1000 ppm group.

In the nonperfused rats, both the brain and spinal cord lesions were described as vacuolation/spongiosis of the white matter. Brain lesions were located primarily in the brainstem (pons and medulla) in the region of the medial longitudinal fasciculus. They were graded minimal to moderate in males and minimal to mild in females. Spinal cord lesions were located in the ventral and lateral funiculi (white matter tracts) and were graded moderate to marked for males and mild to marked for females. One male also had axon degeneration/fragmentation at the same site. Lesions tended to be most severe in the cervical cord and least severe in the thoracic cord, but some lesions were present at all levels in most animals. There were no lesions found in the brain or spinal cords of control group rats or rats in the 100 or 500 ppm groups which were comparable to those in the high concentration group animals. Two males and 1 female from the control group were diagnosed with minimal vacuolation/spongiosis of the brain at different sites than those of chemically-exposed rats. In the males, the lesions were unilateral and located in the cerebellar region. In the female, vacuolation involved the optic chiasm and may have been due to pressure artifact. The brain vacuolation in the control group rats was considered to be an incidental finding.

In the perfused rats, brain and spinal cord lesions were similar in location and nature to those seen in the immersion-fixed animals. Because special stains for myelin and axons were performed, the lesions were further

characterized as myelinopathy and, in several animals, axonopathy in both tissues. Specifically affected sites in the brain included the white matter of the medulla oblongata, pons, and, occasionally, the midbrain, all in the region of the medial longitudinal fasciculus. Also affected in some animals was the white matter around the vestibular nuclei and the trigeminal tracts. Lesions were generally bilateral, although not always symmetrical. All 1000 ppm group rats had myelinopathy and axonopathy in the brainstem (pons and/or medulla). The other sites were affected sporadically in different animals. Brain lesions in males were graded minimal to marked. In females, they were graded minimal to moderate.

As with the nonperfused animals, spinal cord lesions in perfused rats were found in the ventral and lateral funiculi. All the 1000 ppm group animals had both myelinopathy and axonopathy in at least 2 levels of the spinal cord. The cervical level was affected most severely. Myelinopathy was graded mild to marked, and axonopathy was mild to moderate in both sexes. One control group male had minimal grade vacuolation in the dorsal white matter tracts of the spinal cord at all 3 levels. The cause of the lesion in this animal is unknown. As it occurred at a different site within the cord, it is not considered to be comparable to the myelinopathy observed in vinyl pivalate-exposed rats. There were no lesions found in other nervous system tissues, including peripheral nerves, other than those discussed above, which were attributed to chemical exposure. There were no significant lesions of the nervous system in rats exposed to 100 or 500 ppm of vinyl pivalate.

CONCLUSION

Exposure of rats to vinyl pivalate vapor at 1000 ppm produced a minimal to marked myelinopathy and axonopathy of the spinal cord and brain in this test system. Both sexes were equally affected. Lesions were located at characteristic sites, mainly in the brainstem and ventral/lateral funiculi of the spinal cord. There were no lesions in any other tissues, including peripheral nerves, which were attributed to vinyl pivalate exposure. There were no lesions of the nervous system which were attributed to chemical exposure in any rats receiving less than 1000 ppm.

Pathologist:

Patricia E. Losco
Patricia E. Losco, VMD
Diplomate, ACVP

2-10-95
Date

REFERENCES

- Gill, M. W. (1990). Vinyl Pivalate: Single Exposure Oral Neurotoxicity Study in the Rat. BRRC Report 52-133. Bushy Run Research Center, Export, PA.
- Hermansky, S. J., and Benson, C. L. (1994). Vinyl Pivalate: Fourteen-Day Peroral (Gavage) Range-Finding Study in Fischer 344 Rats. BRRC Report 93U1317. Bushy Run Research Center, Export, PA.

TABLE 1
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		10	10	10	10
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
SKIN					
CRUST/SCAB/SCALE		2	2	3	3
SWOLLEN		0	0	0	1
LYMPH ND, S-MAN					
COLOR CHANGE, DIFFUSE		0	1	2	0
SKELETAL MUSCLE					
TRAUMATIZED		1	0	0	0
BRAIN					
MENINGEAL HEMORRHAGE		2	2	0	0
EYE					
TRAUMATIZED		0	0	2	1
LUNGS					
COLOR CHANGE, FOCAL/MULTIFOCAL		0	1	0	0
GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM					

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		10	10	10	10
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
LIVER					
ANOMALY		0	1	0	0
SKIN					
SWOLLEN		1	1	0	2
CRUST/SCAB/SCALE		0	1	1	5
LYMPH ND, S-MAN					
COLOR CHANGE, FOCAL/MULTIFOCAL		2	1	1	2
COLOR CHANGE, DIFFUSE		1	2	2	2
SIZE INCREASE		1	0	0	0
LYMPH ND, OTHER					
SIZE INCREASE		1	0	0	0
THYMIC REGION					
COLOR CHANGE, FOCAL/MULTIFOCAL		4	2	2	0
BRAIN					
MENINGEAL HEMORRHAGE		1	0	0	0
EYE					
TRAUMATIZED		0	0	2	1
HARDERIAN GL					
COLOR CHANGE, DIFFUSE		0	0	0	1
OVARIES					
CYST		0	0	0	1
LUNGS					
COLOR CHANGE, FOCAL/MULTIFOCAL		1	0	0	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		5	5	5	5
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
SKIN					
CRUST/SCAB/SCALE		0	0	1	2
EYE					
TRAUMATIZED		0	0	1	0
GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM					

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF NECROPSY OBSERVATIONS

ANIMALS SACRIFICED AT DAY 12
PERFUSED FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		5	5	5	5
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
BRAIN, NOS					
MENINGEAL HEMORRHAGE		0	1	0	0
SPINAL CORD, CRV					
HEMORRHAGE		1	0	0	0
SKIN					
SWOLLEN		0	0	0	1
EYE					
TRAUMATIZED		2	1	1	0
GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM					

TABLE 5
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		10	10	10	10
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
HEART					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
ORAL/PHARYNGEAL					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
STOMACH					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
LIVER					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
ADRENAL GL					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
SKIN					
TOTAL NUMBER EXAMINED		2	0	0	3
EXAMINED, UNREMARKABLE		2	-	-	2
SUBCUTANEOUS EDEMA		0	-	-	1
MODERATE		0	-	-	1
BLEPHARITIS		0	-	-	1
MODERATE		0	-	-	1
SPLEEN					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
SKELETAL MUSCLE					
TOTAL NUMBER EXAMINED		0	0	0	0
MISSING		1	-	-	-
BRAIN					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		3	4	4	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 5 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	10	10	10	10
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
BRAIN (CONTINUED)				
MENINGEAL HEMORRHAGE	0	1	0	0
MILD	0	1	0	0
BRAIN HEMORRHAGE	0	1	1	0
MINIMAL	0	1	0	0
MILD	0	0	1	0
VACUOLATION/SPONGIOSIS	2	0	0	5
MINIMAL	2	0	0	0
MILD	0	0	0	4
MODERATE	0	0	0	1
SPINAL CORD				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	0
VACUOLATION/SPONGIOSIS	0	0	0	5**
MODERATE	0	0	0	3
MARKED	0	0	0	2
AXON DEGENERATION/FRAGMENTATION	0	0	0	1
MODERATE	0	0	0	1
NERVE, SCIATIC				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
EYE				
TOTAL NUMBER EXAMINED	0	0	0	1
CONJUNCTIVITIS	-	-	-	1
MARKED	-	-	-	1

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

** Significantly different from control group (p < .01)

TABLE 5 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		10	10	10	10
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
EYE (CONTINUED)					
HYPERHEMA/HEMORRHAGE		-	-	-	1
MODERATE		-	-	-	1
KERATITIS		-	-	-	1
MARKED		-	-	-	1
CORNEAL ULCER		-	-	-	1
MARKED		-	-	-	1
HYPOPIYON		-	-	-	1
MARKED		-	-	-	1
TESTES					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
NASAL CAVITY					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	4
DACRYOSOLENITIS		0	-	-	1
MILD		0	-	-	1
LARYNX					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
TRACHEA					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	4
TRACHEITIS		0	-	-	1
MILD		0	-	-	1
LUNGS					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		2	-	-	3

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 5 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		10	10	10	10
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
LUNGS (CONTINUED)					
ALVEOLAR HISTIOCYTOSIS		3	-	-	2
MINIMAL		2	-	-	2
MILD		1	-	-	0
LYMPHOID HYPERPLASIA		0	-	-	1
MILD		0	-	-	1
KIDNEYS					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
URINARY BLADDER					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		3	-	-	4
ECTASIA		0	-	-	1
MODERATE		0	-	-	1
INTRALUMINAL PROTEIN COAGULUM		2	-	-	0
PRESENT		2	-	-	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	10	10	10	10
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
HEART				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
ORAL/PHARYNGEAL				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	4
HEMORRHAGE				
MARKED	0	-	-	1
STOMACH				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
LIVER				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	4	-	-	5
MONONUCLEAR CELL INFILTRATE(S)				
MINIMAL	1	-	-	0
ADRENAL GL				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
SKIN				
TOTAL NUMBER EXAMINED	1	0	0	5
EXAMINED, UNREMARKABLE	1	-	-	5
SPLEEN				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	5	-	-	5
LYMPH ND, S-MAN				
TOTAL NUMBER EXAMINED	4	0	0	4

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 6 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		10	10	10	10
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
LYMPH ND, S-MAN (CONTINUED)					
CYSTIC LYMPHATIC ECTASIA		0	-	-	1
MODERATE		0	-	-	1
SINUS ERYTHROCYTOSIS		4	-	-	4
MILD		0	-	-	1
MODERATE		4	-	-	3
PLASMACYTOSIS		1	-	-	0
MODERATE		1	-	-	0
LYMPH ND, OTHER					
TOTAL NUMBER EXAMINED		1	0	0	0
SINUS ERYTHROCYTOSIS		1	-	-	-
MARKED		1	-	-	-
THYMIC REGION					
TOTAL NUMBER EXAMINED		4	0	0	0
EXAMINED, UNREMARKABLE		1	-	-	-
HEMORRHAGE		3	-	-	-
MILD		1	-	-	-
MODERATE		2	-	-	-
BRAIN					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		3	4	5	0
MENINGEAL HEMORRHAGE		0	1	0	1
MILD		0	1	0	0
MODERATE		0	0	0	1
BRAIN HEMORRHAGE		1	0	0	0
MILD		1	0	0	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 6 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		10	10	10	10
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
BRAIN (CONTINUED)					
VACUOLATION/SPONGIOSIS		1	0	0	5*
MINIMAL		1	0	0	0
MILD		0	0	0	5
SPINAL CORD					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	4	5	0
EPIDERMAL INCLUSION CYST					
PRESENT		0	1	0	0
VACUOLATION/SPONGIOSIS		0	0	0	5**
MILD		0	0	0	1
MODERATE		0	0	0	3
MARKED		0	0	0	1
NERVE, SCIATIC					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
EYE					
TOTAL NUMBER EXAMINED		0	0	0	1
RETROORBITAL HEMORRHAGE					
MILD		-	-	-	1
HARDERIAN GL		-	-	-	1
TOTAL NUMBER EXAMINED		0	0	0	1
FIBROSIS					
MILD		-	-	-	1
OVARIES					
TOTAL NUMBER EXAMINED		0	0	0	1
EXAMINED, UNREMARKABLE		-	-	-	1
NASAL CAVITY					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	3

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

* Significantly different from control group (p < .05)
** Significantly different from control group (p < .01)

TABLE 6 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	10	10	10	10
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
NASAL CAVITY (CONTINUED)				
HEMORRHAGE	0	-	-	1
MILD	0	-	-	1
RHINITIS	0	-	-	1
MILD	0	-	-	1
LARYNX				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	3	-	-	5
ASPIRATED BLOOD	1	-	-	0
MILD	1	-	-	0
LARYNGITIS	1	-	-	0
MILD	1	-	-	0
TRACHEA				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	4	-	-	5
ASPIRATED BLOOD	1	-	-	0
MILD	1	-	-	0
LUNGS				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	3	-	-	3
ALVEOLAR HISTIOCYTOSIS	1	-	-	1
MINIMAL	0	-	-	1
MILD	1	-	-	0
HEMORRHAGE	0	-	-	1
MILD	0	-	-	1

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 6 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 13
NONPERFUSED FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		10	10	10	10
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
LUNGS (CONTINUED)					
INTERSTITIAL PNEUMONITIS		1	-	-	0
MINIMAL		1	-	-	0
KIDNEYS					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		4	-	-	3
MINERALIZATION		1	-	-	2
MINIMAL		1	-	-	2
URINARY BLADDER					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 7

VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
TISSUE ABBREVIATIONS USED FOR NEUROPATHOLOGY EVALUATION

[ABBREVIATION;ABBREVIATED NAME IN THE COMPUTER;COMPLETE NAME]

OLFACTORY BULB;OLFACTORY BULB	SPINAL CORD, LUM;SPINAL CORD, LUMBAR
PIRIFORM CORTEX;PIRIFORM CORTEX	SPINAL NERVE RTS;SPINAL NERVE ROOTS
FRONTAL CORTEX;FRONTAL CORTEX	DORSAL ROOT GANG;DORSAL ROOT GANGLIA
ANT COMMISSURE;ANTERIOR COMMISSURE	GASSERIAN GANG;GASSERIAN GANGLIA
SEPTAL NUCLEI;SEPTAL NUCLEI	SCIATIC NERVE;SCIATIC NERVE
CAUD NUC/PUTAMEN;CAUDATE NUCLEUS/PUTAMEN	TIBIAL NERVE;TIBIAL NERVE
GLOBUS PALLIDUS;GLOBUS PALLIDUS	PERONEAL/SURAL N;PERONEAL/SURAL NERVE
EXTERNAL CAPSULE;EXTERNAL CAPSULE	CEREBRAL CORTEX;CEREBRAL CORTEX
CORPUS CALLOSUM;CORPUS CALLOSUM	SUBCORT AREA NOS;SUBCORTICAL AREAS, NOS
FORNIX;FORNIX	CLAUSTRUM;CLAUSTRUM
OPTIC N/CHIASM;OPTIC NERVE/CHIASM	SUBICULUM;SUBICULUM
INTERNAL CAPSULE;INTERNAL CAPSULE	FIMBRIA;FIMBRIA
THALAMUS;THALAMUS	HIPPOCAMPUS, CA1;HIPPOCAMPUS, CA1
HYPOTHALAMUS;HYPOTHALAMUS	HIPPOCAMPUS, CA2;HIPPOCAMPUS, CA2
AMYGDALA;AMYGDALA	HIPPOCAMPUS, CA3;HIPPOCAMPUS, CA3
HIPPOCAMPUS;HIPPOCAMPUS	HIPPOCAMPUS, CA4;HIPPOCAMPUS, CA4
PARIETAL CORTEX;PARIETAL CORTEX	DENTATE GYRUS;DENTATE GYRUS
TEMPORAL CORTEX;TEMPORAL CORTEX	BRAIN, NOS;BRAIN, NOS
OCCIPITAL CORTEX;OCCIPITAL CORTEX	WHITE MATTER NOS;WHITE MATTER, NOS
MENINGES;MENINGES	PYRAMIDS;PYRAMIDS
MIDBRAIN;MIDBRAIN	STRIA MEDULLARIS.;STRIA MEDULLARIS
SUBSTANTIA NIGRA;SUBSTANTIA NIGRA	LONG. FASCICULUS;LONGITUDINAL FASCICULUS
CEREBELLAR CTX;CEREBELLAR CORTEX	POST COMMISSURE;POSTERIOR COMMISSURE
CEREBELLAR W.M.;CEREBELLAR WHITE MATTER	CEREBRAL PED;CEREBRAL PEDUNCLE
CEREBELLAR NUC;CEREBELLAR NUCLEI	DENTATE NUCLEUS;DENTATE NUCLEUS
VESTIBULAR NUC;VESTIBULAR NUCLEUS	FASTIGIAL NUC;FASTIGIAL NUCLEUS
PONS;PONS	CEREBELLAR PEDS;CEREBELLAR PEDUNCLES
MEDULLA OBL;MEDULLA OBLONGATA	OLFACTORY TRACT;OLFACTORY TRACT
TRIGEMINAL TRACT ;TRIGEMINAL TRACT	PINEAL GLAND;PINEAL GLAND
SPINAL CORD, CRV,;SPINAL CORD, CERVICAL	PARAVENT ORGAN;PARAVENTRICULAR ORGAN(S)
SPINAL CORD, THR;SPINAL CORD, THORACIC	CRANIAL N, NOS;CRANIAL NERVE, NOS
	NERVE OTHER;NERVE, OTHER

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		5	5	5	5
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
MENINGES					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
PIRIFORM CORTEX					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
FRONTAL CORTEX					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
PARIETAL CORTEX					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
TEMPORAL CORTEX					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
OCCIPITAL CORTEX					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
SEPTAL NUCLEI					
TOTAL NUMBER EXAMINED		4	5	3	3
EXAMINED, UNREMARKABLE		4	5	3	3
MISSING		1	0	2	2
CAUD NUC/PUTAMEN					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
GLOBUS PALLIDUS					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
AMYGDALA					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
HIPPOCAMPUS					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 8 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
THALAMUS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
HYPOTHALAMUS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
MIDBRAIN				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	2
MYELINOPATHY	0	0	0	3
MINIMAL	0	0	0	2
MILD	0	0	0	1
SUBSTANTIA NIGRA				
TOTAL NUMBER EXAMINED	5	5	5	4
EXAMINED, UNREMARKABLE	5	5	5	4
MISSING	0	0	0	1
CEREBELLAR W.M.				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
ANT COMMISSURE				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
EXTERNAL CAPSULE				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
INTERNAL CAPSULE				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
CORPUS CALLOSUM				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
FORNIX				
TOTAL NUMBER EXAMINED	3	5	2	1
EXAMINED, UNREMARKABLE	3	5	2	1
MISSING	2	0	3	4

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 8 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
CEREBELLAR CTX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
CEREBELLAR NUC				
TOTAL NUMBER EXAMINED	5	5	5	4
EXAMINED, UNREMARKABLE	5	5	5	4
MISSING	0	0	0	1
VESTIBULAR NUC				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	1
MYELINOPATHY	0	0	0	4*
MINIMAL	0	0	0	1
MILD	0	0	0	3
PONS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	0
MYELINOPATHY	0	0	0	5**
MILD	0	0	0	1
MODERATE	0	0	0	4
AXONOPATHY	0	0	0	5**
MILD	0	0	0	1
MODERATE	0	0	0	4
MEDULLA OBL				
TOTAL NUMBER EXAMINED	5	4	5	5
EXAMINED, UNREMARKABLE	5	4	5	0
MISSING	0	1	0	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

* Significantly different from control group (p < .05)
** Significantly different from control group (p < .01)

TABLE 8 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
MEDULLA OBL (CONTINUED)				
MYELINOPATHY	0	0	0	5**
MODERATE	0	0	0	3
MARKED	0	0	0	2
AXONOPATHY	0	0	0	4*
MILD	0	0	0	1
MODERATE	0	0	0	3
OLFACTORY BULB				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
OPTIC N/CHIASM				
TOTAL NUMBER EXAMINED	5	3	5	5
EXAMINED, UNREMARKABLE	5	3	5	5
MISSING	0	2	0	0
TRIGEMINAL TRACT				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	3
MYELINOPATHY	0	0	0	2
MINIMAL	0	0	0	2
AXONOPATHY	0	0	0	1
MINIMAL	0	0	0	1
SPINAL CORD, CRV				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	4	5	5	0
VACUOLATION	1	0	0	0
MINIMAL	1	0	0	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

* Significantly different from control group (p < .05)
** Significantly different from control group (p < .01)

TABLE 8 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
SPINAL CORD, CRV(CONTINUED)				
MYELINOPATHY	0	0	0	5**
MODERATE	0	0	0	1
MARKED	0	0	0	4
AXONOPATHY	0	0	0	5**
MODERATE	0	0	0	5
SPINAL CORD, THR				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	4	5	5	0
VACUOLATION	1	0	0	0
MINIMAL	1	0	0	0
MYELINOPATHY	0	0	0	5**
MODERATE	0	0	0	2
MARKED	0	0	0	3
AXONOPATHY	0	0	0	5**
MODERATE	0	0	0	5
SPINAL CORD, LUM				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	4	5	5	0
VACUOLATION	1	0	0	0
MINIMAL	1	0	0	0
MYELINOPATHY	0	0	0	5**
MILD	0	0	0	3
MODERATE	0	0	0	2

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

** Significantly different from control group (p < .01)

TABLE 8 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 11
PERFUSED MALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		5	5	5	5
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
SPINAL CORD, LUM(CONTINUED)					
AXONOPATHY		0	0	0	3
MILD		0	0	0	2
MODERATE		0	0	0	1
SPINAL NERVE RTS					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
DORSAL ROOT GANG					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
GASSERIAN GANG					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		4	-	-	5
HEMORRHAGE		1	-	-	0
MILD		1	-	-	0
SCIATIC NERVE					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
TIBIAL NERVE					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
PERONEAL/SURAL N					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 9
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE
ANIMALS SACRIFICED AT DAY 12
PERFUSED FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		5	5	5	5
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
MENINGES					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
PIRIFORM CORTEX					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
FRONTAL CORTEX					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
PARIETAL CORTEX					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
TEMPORAL CORTEX					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
OCCIPITAL CORTEX					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
SEPTAL NUCLEI					
TOTAL NUMBER EXAMINED		5	4	4	5
EXAMINED, UNREMARKABLE		5	4	4	5
MISSING		0	1	1	0
CAUD NUC/PUTAMEN					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
GLOBUS PALLIDUS					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
AMYGDALA					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5
HIPPOCAMPUS					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	5

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 9 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 12
PERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
THALAMUS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
HYPOTHALAMUS				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
MIDBRAIN				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	2
MYELINOPATHY	0	0	0	3
MINIMAL	0	0	0	3
SUBSTANTIA NIGRA				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
CEREBELLAR W.M.				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
ANT COMMISSURE				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
EXTERNAL CAPSULE				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
INTERNAL CAPSULE				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
CORPUS CALLOSUM				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
FORNIX				
TOTAL NUMBER EXAMINED	3	3	2	4
EXAMINED, UNREMARKABLE	3	3	2	4
MISSING	2	2	3	1

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

None significantly different from control group

TABLE 9 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 12
PERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
CEREBELLAR CTX				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
CEREBELLAR NUC				
TOTAL NUMBER EXAMINED	5	3	5	5
EXAMINED, UNREMARKABLE	5	3	5	5
MISSING	0	2	0	0
VESTIBULAR NUC				
TOTAL NUMBER EXAMINED	5	4	5	5
EXAMINED, UNREMARKABLE	5	4	5	0
MISSING	0	1	0	0
MYELINOPATHY	0	0	0	5**
MINIMAL	0	0	0	1
MILD	0	0	0	3
MODERATE	0	0	0	1
AXONOPATHY	0	0	0	3
MILD	0	0	0	3
PONS				
TOTAL NUMBER EXAMINED	5	4	5	5
EXAMINED, UNREMARKABLE	5	4	5	0
MISSING	0	1	0	0
MYELINOPATHY	0	0	0	5**
MODERATE	0	0	0	5
AXONOPATHY	0	0	0	5**
MILD	0	0	0	2
MODERATE	0	0	0	3
MEDULLA OBL				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

** Significantly different from control group (p < .01)

TABLE 9 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 12
PERFUSED FEMALES

GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	5	5	5	5
NUMBER OF ANIMALS SACRIFICED	5	5	5	5
MEDULLA OBL (CONTINUED)				
MYELINOPATHY	0	0	0	5**
MODERATE	0	0	0	5
AXONOPATHY	0	0	0	5**
MODERATE	0	0	0	5
OLFACTORY BULB				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	5
OPTIC N/CHIASM				
TOTAL NUMBER EXAMINED	5	5	5	3
EXAMINED, UNREMARKABLE	5	5	5	3
MISSING	0	0	0	2
TRIGEMINAL TRACT				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	2
MYELINOPATHY	0	0	0	3
MINIMAL	0	0	0	3
SPINAL CORD, CRV				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	0
MYELINOPATHY	0	0	0	5**
MODERATE	0	0	0	1
MARKED	0	0	0	4
AXONOPATHY	0	0	0	5**
MODERATE	0	0	0	5
SPINAL CORD, THR				
TOTAL NUMBER EXAMINED	5	5	5	5
EXAMINED, UNREMARKABLE	5	5	5	0

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

** Significantly different from control group (p < .01)

TABLE 9 (Continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

SUMMARY OF MICROSCOPIC DIAGNOSES BY GRADE

ANIMALS SACRIFICED AT DAY 12
PERFUSED FEMALES

	GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP		5	5	5	5
NUMBER OF ANIMALS SACRIFICED		5	5	5	5
SPINAL CORD, THR(CONTINUED)					
MYELINOPATHY		0	0	0	5**
MARKED		0	0	0	5
AXONOPATHY		0	0	0	5**
MODERATE		0	0	0	5
SPINAL CORD, LUM					
TOTAL NUMBER EXAMINED		5	5	5	5
EXAMINED, UNREMARKABLE		5	5	5	0
MYELINOPATHY		0	0	0	5**
MILD		0	0	0	4
MODERATE		0	0	0	1
AXONOPATHY		0	0	0	2
MILD		0	0	0	1
MODERATE		0	0	0	1
SPINAL NERVE RTS					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
DORSAL ROOT GANG					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
GASSERIAN GANG					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
SCIATIC NERVE					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
TIBIAL NERVE					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5
PERONEAL/SURAL N					
TOTAL NUMBER EXAMINED		5	0	0	5
EXAMINED, UNREMARKABLE		5	-	-	5

GROUP LEGEND: 1 is 0 PPM, 2 is 100 PPM, 3 is 500 PPM, 4 is 1000 PPM

** Significantly different from control group (p < .01)

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats
Clinical Pathology Report
(9 Pages)

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SUMMARY

Male and female Fischer 344 rats were exposed to vinyl pivalate (0, 100, 500, or 1000 ppm) by vapor inhalation 6 hours/day, for 5 consecutive days for the first week and 3, 4, or 5 days the following week. Blood samples were collected for clinical pathology evaluation following the eighth exposure for males and the ninth exposure for females.

Male rats in the 500 and 1000 ppm groups and female rats in the 100, 500, and 1000 ppm groups had concentration dependent decreases in erythrocyte counts, hemoglobin, and hematocrit values. Male and female rats in the 1000 ppm groups also had decreases in mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) values. This was interpreted as a hypochromic, normocytic anemia based on the erythrocyte parameters.

MATERIALS AND METHODS

In this study, male and female Fischer 344 rats were exposed to vinyl pivalate by vapor inhalation 6 hours/day, for 5 consecutive days the first week and 3, 4, or 5 days the following week. Target concentrations were 0 (control), 100, 500, and 1000 ppm.

Blood samples for all hematology analyses were collected by retroorbital bleeding from anesthetized rats following the eighth exposure for males and the ninth exposure for females. Rats were not considered to be fasted prior to bleeding. All analyses were performed in a predetermined alternating (1 animal from each group, then repeating) order.

Hematology

Approximately 0.5 ml of blood was collected into blood collection tubes containing EDTA as an anticoagulant for the hematologic determinations.

The following hematologic parameters were measured or calculated: erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count, leukocyte count, segmented neutrophils, lymphocytes, monocytes, basophils, and eosinophils. These hematologic analyses were performed on a COBAS HELIOSTM SDIFF on the day of the sample collection. Commercially available quality control samples were analyzed prior to the animal samples. Blood smears for differential leukocyte counts were prepared for all animals. The smears were not evaluated unless a value was not obtained from the instrument, to confirm the instrument results, or differentiate unusual patterns of cell populations. The source of the data is documented in the raw data.

Data Analyses

The results of the hematology analyses for quantitative, continuous variables were intercompared for the exposure and the control group by Levene's test for equality of variances, analysis of variance (ANOVA), and t-tests. If the

ANOVA indicated statistical significance among experimental groups, the t-test was used to delineate which groups differ from the control group. If Levene's test indicated homogeneity of variances, the group was compared by an ANOVA for equal variances followed, when appropriate, by pooled variance t-tests. If Levene's test indicated heterogeneity of variances, the groups were compared by an ANOVA for unequal variances followed, when appropriate, by a separate variance t-test.

All statistical analyses were performed using BMDP Statistical Software (Dixon, 1990). The probability value of less than 0.05 (two-tailed) was used as the critical level of significance for all tests.

RESULTS AND DISCUSSION

All references to differences in group mean values in the following text refer to comparisons of statistically significant differences between the exposure group and the control group, unless otherwise noted. Repeated reference to the control and the statistical significance will not be made in order to simplify the text.

The summary results of hematology determinations for male and female rats are presented in Tables 1-2. The individual results for these animals are included in Appendix 9.

Male rats in the 500 and 1000 ppm groups and female rats in the 100, 500, and 1000 ppm groups had decreases in erythrocyte counts, hemoglobin, and hematocrit values. Male and female rats in the 1000 ppm groups also had decreases in MCH and MCHC values. Male rats in the 1000 ppm group had an increase in total leukocytes and lymphocytes, while female rats in the 1000 ppm group had a decrease in lymphocytes. Since there was an inconsistent change in the leukocyte and lymphocyte counts between male and female rats, these differences were not believed to be related to exposure to vinyl pivalate. Male rats in the 1000 ppm group had a slight increase in platelets probably associated with the increase in lymphocytes, but not considered to be biologically significant. The slight decrease in basophils in female rats in the 100 and 1000 ppm groups was not considered to be exposure related since the control values were greater than the normal range for this species.

CONCLUSION

Male and female rats exposed to vinyl pivalate developed a hypochromic microcytic anemia within 10 days of exposure. Male rats in the 500 and 1000 ppm groups and female rats in the 100, 500, and 1000 ppm groups had decreases in erythrocyte counts, hemoglobin, and hematocrit values. Male and female rats in the 1000 ppm groups also had decreases in MCH and MCHC values. This was interpreted as a hypochromic, normocytic anemia based on the erythrocyte parameters.

Clinical Pathologist:

Douglas A. Neptun
Douglas A. Neptun, B.S., CC(NRCC), MT(ASCP)

2/10/95

Date

REFERENCE

Dixon, W. J. (1990). BMDP Statistical Software. University of California Press, Berkeley, CA.

TABLE 1
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 10

MALES				
GROUP: FPM	0	100	500	1000
ERYTHROCYTES ($10^6/\mu\text{l}$)				
MEAN	7.82	7.71	7.43**	7.27**
S.D.	0.166	0.199	0.305	0.217
N	10	10	10	10
HEMOGLOBIN (g/dl)				
MEAN	15.2	15.1	14.4**	13.7**
S.D.	0.28	0.36	0.50	0.35
N	10	10	10	10
HEMATOCRIT (%)				
MEAN	43.7	43.1	41.6**	40.2**
S.D.	0.76	0.95	1.37	1.35
N	10	10	10	10
MEAN CORPUSCULAR VOLUME (μm^3)				
MEAN	56.	56.	56.	55.
S.D.	0.6	0.5	0.8	0.5
N	10	10	10	10
MEAN CORPUSCULAR HEMOGLOBIN (pg)				
MEAN	19.4	19.6	19.4	18.8**
S.D.	0.21	0.27	0.29	0.24
N	10	10	10	10
MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)				
MEAN	34.7	35.0	34.6	34.0**
S.D.	0.43	0.37	0.38	0.50
N	10	10	10	10
PLATELETS ($10^3/\mu\text{l}$)				
MEAN	663.	633.	636.	745.**
S.D.	35.5	49.7	44.0	60.7
N	9	10	9	9
LEUKOCYTES ($10^3/\mu\text{l}$)				
MEAN	6.2	6.5	6.1	7.3*
S.D.	1.18	0.38	0.16	0.73
N	10	10	10	10
SEGMENTED NEUTROPHILS ($10^3/\mu\text{l}$)				
MEAN	0.61	0.54	0.49	0.57
S.D.	0.367	0.103	0.107	0.174
N	10	10	10	10
LYMPHOCYTES ($10^3/\mu\text{l}$)				
MEAN	5.39	5.76	5.50	6.53**
S.D.	0.815	0.347	0.175	0.607
N	10	10	10	10
MONOCYTES ($10^3/\mu\text{l}$)				
MEAN	0.04	0.08	0.03	0.06
S.D.	0.033	0.097	0.052	0.094
N	10	10	10	10

* Significantly different from control group ($p < .05$)
** Significantly different from control group ($p < .01$)

TABLE 1 (continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 10

MALES				
GROUP: PPM	0	100	500	1000
BASOPHILS ($10^3/\mu\text{l}$)				
MEAN	0.07	0.05	0.07	0.07
S.D.	0.028	0.029	0.028	0.033
N	10	10	10	10
EOSINOPHILS ($10^3/\mu\text{l}$)				
MEAN	0.05	0.03	0.06	0.04
S.D.	0.054	0.015	0.049	0.018
N	10	10	10	10
BANDIED NEUTROPHILS ($10^3/\mu\text{l}$)				
MEAN		0.00	0.00	0.00
S.D.		0.000	0.000	0.000
N		1	1	1
LARGE MONONUCLEAR CELLS ($10^3/\mu\text{l}$)				
MEAN		0.00	0.00	0.00
S.D.		0.000	0.000	0.000
N		1	1	1
LARGE GRANULAR LYMPHOCYTES ($10^3/\mu\text{l}$)				
MEAN		0.00	0.00	0.00
S.D.		0.000	0.000	0.000
N		1	1	1
IMMATURE GRANULOCYTES ($10^3/\mu\text{l}$)				
MEAN		0.00	0.00	0.00
S.D.		0.000	0.000	0.000
N		1	1	1
NUCLEATED RBCs (cells/100 WBCs)				
MEAN		1.	7.	4.
S.D.		0.0	0.0	0.0
N		1	1	1
None significantly different from control group				

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 11

FEMALES				
GROUP: PPM	0	100	500	1000
ERYTHROCYTES ($10^6/\mu\text{l}$)				
MEAN	7.81	7.51**	7.39**	7.39**
S.D.	0.237	0.167	0.144	0.285
N	9	10	10	10
HEMOGLOBIN (g/dl)				
MEAN	15.4	15.0*	14.4**	14.1**
S.D.	0.47	0.20	0.23	0.50
N	9	10	10	10
HEMATOCRIT (%)				
MEAN	43.2	41.6**	40.9**	40.5**
S.D.	1.25	0.76	0.75	1.78
N	9	10	10	10
MEAN CORPUSCULAR VOLUME (μm^3)				
MEAN	55.	55.	55.	55.
S.D.	0.5	0.5	0.5	0.6
N	9	10	10	10
MEAN CORPUSCULAR HEMOGLOBIN (pg)				
MEAN	19.7	19.9	19.5	19.0**
S.D.	0.28	0.38	0.40	0.24
N	9	10	10	10
MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)				
MEAN	35.6	36.0	35.3	34.7**
S.D.	0.75	0.50	0.75	0.59
N	9	10	10	10
PLATELETS ($10^3/\mu\text{l}$)				
MEAN	625.	617.	649.	677.
S.D.	31.1	58.1	67.5	64.7
N	9	10	7	10
LEUKOCYTES ($10^3/\mu\text{l}$)				
MEAN	7.5	6.7	8.2	6.7
S.D.	0.93	0.74	0.88	1.19
N	9	10	10	10
SEGMENTED NEUTROPHILS ($10^3/\mu\text{l}$)				
MEAN	0.70	0.66	0.82	0.73
S.D.	0.195	0.215	0.224	0.235
N	9	10	10	10
LYMPHOCYTES ($10^3/\mu\text{l}$)				
MEAN	6.64	5.91	7.22	5.81*
S.D.	0.751	0.593	0.678	1.054
N	9	10	10	10
MONOCYTES ($10^3/\mu\text{l}$)				
MEAN	0.04	0.07	0.04	0.07
S.D.	0.033	0.084	0.017	0.065
N	9	10	10	10

* Significantly different from control group ($p < .05$)

** Significantly different from control group ($p < .01$)

TABLE 2 (continued)
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
SUMMARY OF HEMATOLOGY
DAY 11

FEMALES				
GROUP: PPM	0	100	500	1000
BASOPHILS ($10^3/\mu\text{l}$)				
MEAN	0.07	0.05*	0.07	0.03**
S.D.	0.022	0.021	0.019	0.027
N	9	10	10	10
EOSINOPHILS ($10^3/\mu\text{l}$)				
MEAN	0.04	0.05	0.08	0.06
S.D.	0.011	0.055	0.045	0.063
N	9	10	10	10
BANDED NEUTROPHILS ($10^3/\mu\text{l}$)				
MEAN		0.00		0.00
S.D.		0.000		0.000
N		1		3
LARGE MONONUCLEAR CELLS ($10^3/\mu\text{l}$)				
MEAN		0.00		0.00
S.D.		0.000		0.000
N		1		3
LARGE GRANULAR LYMPHOCYTES ($10^3/\mu\text{l}$)				
MEAN		0.00		0.00
S.D.		0.000		0.000
N		1		3
IMMATURE GRANULOCYTES ($10^3/\mu\text{l}$)				
MEAN		0.00		0.00
S.D.		0.000		0.000
N		1		3
NUCLEATED RBCs (cells/100 WBCs)				
MEAN		0.		2.
S.D.		0.0		1.5
N		1		3
* Significantly different from control group (p < .05)				
** Significantly different from control group (p < .01)				

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

Individual Clinical Observation Data

(11 Pages)

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TABLE 1
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATION DATA

ABBREVIATIONS

The following is a list of three letter abbreviations for locations of clinical signs that may appear in this appendix.

ABD ABDOMEN	LHL LEG-HIND-LEFT
ANS ANUS	LHR LEG-HIND-RIGHT
AXB AXILLA-BOTH	LNS LOCATION NOT SPECIFIED
AXL AXILLA-LEFT	MTH MOUTH
AXR AXILLA-RIGHT	MUL MULTIPLE AREAS, NOS*
BCK BACK	NCK NECK
BDY ENTIRE BODY	NSE NOSE
CHS CHEST	PAL PAWS-ALL
EAB EAR-BOTH	PFB PAW-FORE-BOTH
EAL EAR-LEFT	PFL PAW-FORE-LEFT
EAR EAR-RIGHT	PFR PAW-FORE-RIGHT
ELB EYELID-BOTH	PHB PAW-HIND-BOTH
ELL EYELID-LEFT	PHL PAW-HIND-LEFT
ELR EYELID-RIGHT	PHR PAW-HIND-RIGHT
ETB EYE-BOTH	PNS PENIS
EYL EYE-LEFT	SCR SCROTUM
EYR EYE-RIGHT	SDB SIDE-BOTH
FAC FACE	SDL SIDE-LEFT
GEN GENITAL	SDR SIDE-RIGHT
HED HEAD	SHB SHOULDER-BOTH
HPB HIP-BOTH	SHL SHOULDER-LEFT
HPL HIP-LEFT	SHR SHOULDER-RIGHT
HPR HIP-RIGHT	TAL TAIL
INB INGUINAL-BOTH	TEE TEETH
INL INGUINAL-LEFT	TRA TREATMENT AREA
INR INGUINAL-RIGHT	TSB TESTIS-BOTH
LAL LEGS-ALL	TSL TESTIS-LEFT
LFB LEG-FORE-BOTH	TSR TESTIS-RIGHT
LFL LEG-FORE-LEFT	VAG VAGINA
LFR LEG-FORE-RIGHT	*NOS NOT OTHERWISE SPECIFIED
LHB LEG-HIND-BOTH	

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
0 PPM	717	NORMAL	10	1- 10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
		EYES/EARS/NOSE	1	11	PERINASAL ENCRUSTATION
	735	NORMAL	12	1- 12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
	752	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	2	12- 13	PERINASAL ENCRUSTATION
	715	NORMAL	10	1- 10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
		EYES/EARS/NOSE	1	11	PROCEDURAL TRAUMA (EYL 1)
	711	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	12	PERINASAL ENCRUSTATION
	750	NORMAL	10	1- 10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
100 PPM	751	NORMAL	10	1- 10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
	706	NORMAL	10	1- 10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	3	11- 13	PERINASAL ENCRUSTATION
	738	NORMAL	1	11	PROCEDURAL TRAUMA (EYL 1)
		FATE	10	1- 10	NO SIGNIFICANT CLINICAL OBSERVATIONS
	728	NORMAL	12	1- 12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
	740	NORMAL	12	1- 12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
	714	NORMAL	12	1- 12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
	745	NORMAL	10	1- 10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
	703	NORMAL	10	1- 10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
	725	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	2	12- 13	PERINASAL ENCRUSTATION
	709	NORMAL	10	1- 10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
	755	NORMAL	10	1- 10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
	716	NORMAL	10	1- 10	NO SIGNIFICANT CLINICAL OBSERVATIONS

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
100 PPM					
	716	FATE EYES/EARS/NOSE	1	13	SCHEDULED SACRIFICE
			3	11-13	PERIOcular ENCRUSTATION (EYR 3)
	736	NORMAL	12	1-12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
	719	NORMAL	10	1-10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
500 PPM					
	743	NORMAL	10	1-10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
		EYES/EARS/NOSE	1	11	PERINASAL ENCRUSTATION
	757	NORMAL	12	1-12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
	720	NORMAL	12	1-12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	3	11-13	PROCEDURAL TRAUMA (EYL 3)
			1	13	PERIOcular ENCRUSTATION (EYL 1)
	710	NORMAL	10	1-10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
	731	NORMAL	10	1-10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
		EYES/EARS/NOSE	1	11	PERINASAL ENCRUSTATION
	730	NORMAL	11	1-11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	2	12-13	PERINASAL ENCRUSTATION
			1	12	PERIOcular ENCRUSTATION (EYB 1)
			1	11	PROCEDURAL TRAUMA (EYL 1)
	722	NORMAL	10	1-10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
		EYES/EARS/NOSE	1	11	PROCEDURAL TRAUMA (EYL 1)
	721	NORMAL	10	1-10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	11	SCHEDULED PERFUSION SACRIFICE
		EYES/EARS/NOSE	1	11	PERINASAL ENCRUSTATION
			2	10-11	SWOLLEN PERIOcular TISSUE (EYB 2)
			1	10	PERIOcular ENCRUSTATION (EYL 1)
	713	NORMAL	12	1-12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
	724	NORMAL	10	1-10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	3	11-13	PERINASAL ENCRUSTATION
			1	12	PERIOcular ENCRUSTATION (EYL 1)
1000 PPM					
	733	NORMAL	5	1-8	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
1000 PPM					
733	BEHAVIOR/CNS EYES/EARS/NOSE	16	2-12	INCOORDINATION	
		3	12-13	PERIOCLAR ENCRUSTATION (EYB 1, EYR 2)	
		1	11	PROCEDURAL TRAUMA (EYR 1)	
729	NORMAL	2	9-10	SWOLLEN PERIOCLAR TISSUE (EYB 2)	
	FATE	5	1-8	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	BEHAVIOR/CNS	1	11	SCHEDULED PERFUSION SACRIFICE	
	EYES/EARS/NOSE	13	2-11	INCOORDINATION	
		6	4-10	SWOLLEN PERIOCLAR TISSUE (EYB 2, EYL 4)	
		4	4-5	PERIOCLAR ENCRUSTATION (EYL 4)	
		2	4	PALE EYES (EYL 2)	
712	NORMAL	5	1-8	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	11	SCHEDULED PERFUSION SACRIFICE	
	BEHAVIOR/CNS	13	2-11	INCOORDINATION	
	EYES/EARS/NOSE	4	5-11	SWOLLEN PERIOCLAR TISSUE (EYB 3, EYR 1)	
		4	4-5	PERIOCLAR ENCRUSTATION (EYB 4)	
727	NORMAL	4	1-8	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	11	SCHEDULED PERFUSION SACRIFICE	
	BEHAVIOR/CNS	13	2-11	INCOORDINATION	
	EYES/EARS/NOSE	5	4-8	PERIOCLAR ENCRUSTATION (EYB 4, EYL 1)	
739	NORMAL	6	1-9	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	11	SCHEDULED PERFUSION SACRIFICE	
	BEHAVIOR/CNS	11	2-11	INCOORDINATION	
	EYES/EARS/NOSE	2	9-10	SWOLLEN PERIOCLAR TISSUE (EYB 2)	
744	NORMAL	5	1-8	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	13	SCHEDULED SACRIFICE	
	BEHAVIOR/CNS	16	2-12	INCOORDINATION	
	EYES/EARS/NOSE	3	9-10	SWOLLEN PERIOCLAR TISSUE (EYB 3)	
		4	4-5	PERIOCLAR ENCRUSTATION (EYR 4)	
737	NORMAL	5	1-8	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	13	SCHEDULED SACRIFICE	
	BEHAVIOR/CNS	16	2-12	INCOORDINATION	
	EYES/EARS/NOSE	2	11-13	PROCEDURAL TRAUMA (EYR 2)	
		5	4-13	PERIOCLAR ENCRUSTATION (EYR 5)	
		5	4-10	SWOLLEN PERIOCLAR TISSUE (EYB 5)	
723	NORMAL	7	1-9	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	13	SCHEDULED SACRIFICE	
	BEHAVIOR/CNS	13	2-12	INCOORDINATION	
	EYES/EARS/NOSE	1	11	PROCEDURAL TRAUMA (EYR 1)	
		1	10	SWOLLEN PERIOCLAR TISSUE (EYB 1)	
732	NORMAL	5	1-8	NO SIGNIFICANT CLINICAL OBSERVATIONS	
	FATE	1	11	SCHEDULED PERFUSION SACRIFICE	
	BEHAVIOR/CNS	13	2-11	INCOORDINATION	
	EYES/EARS/NOSE	1	11	PERIOCLAR ENCRUSTATION (EYR 1)	

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
MALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
1000 PPM	732	EYES/EARS/NOSE	2	9- 11	SWOLLEN PERIOCCULAR TISSUE (EVB 1, EYR 1)
	746	NORMAL	5	1- 8	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		BEHAVIOR/CNS	16	2- 12	INCOORDINATION
		EYES/EARS/NOSE	7	4- 13	PERIOCCULAR ENCRUSTATION (EYR 7)
			1	10	SWOLLEN PERIOCCULAR TISSUE (EVB 1)

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
0 PPM	800	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
	764	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	12	PROCEDURAL TRAUMA (EYR 1)
	803	NORMAL	12	1- 12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
	801	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
		EYES/EARS/NOSE	1	12	PROCEDURAL TRAUMA (EYR 1)
	784	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	12	SWOLLEN PERIOCTULAR TISSUE (EYR 1)
	783	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	12	PROCEDURAL TRAUMA (EYR 1)
100 PPM	778	NORMAL	12	1- 12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
	777	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
	775	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
		BODY	1	12	URINE STAINS
	809	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
		EYES/EARS/NOSE	1	12	PROCEDURAL TRAUMA (EYR 1)
	797	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
		EYES/EARS/NOSE	1	12	PERINASAL ENCRUSTATION
	810	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
	793	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	2	12- 13	PROCEDURAL TRAUMA (EYL 2)
	789	NORMAL	12	1- 12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
	780	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	1	12	PROCEDURAL TRAUMA (EYL 1)
		FATE	1	12	PERIOCTULAR ENCRUSTATION (EYL 1)
	779	NORMAL	11	1- 11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
100 PPM	779	EYES/EARS/NOSE	1	13	SWOLLEN PERIOCLAR TISSUE (EYR 1)
			1	12	PROCEDURAL TRAUMA (EYL 1)
	807	NORMAL	11	1-11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
		EYES/EARS/NOSE	1	12	PROCEDURAL TRAUMA (EYL 1)
	785	NORMAL	11	1-11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
		EYES/EARS/NOSE	1	12	PROCEDURAL TRAUMA (EYL 1)
	772	NORMAL	12	1-12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
500 PPM	799	NORMAL	11	1-11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
	770	NORMAL	12	1-12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
	805	NORMAL	11	1-11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
		EYES/EARS/NOSE	2	12-13	PROCEDURAL TRAUMA (EYR 2)
	788	NORMAL	11	1-11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
	806	NORMAL	12	1-12	NO SIGNIFICANT CLINICAL OBSERVATIONS
	808	NORMAL	11	1-11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
	762	NORMAL	11	1-11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
	791	NORMAL	12	1-12	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
	771	NORMAL	11	1-11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
	774	EYES/EARS/NOSE	1	12	PROCEDURAL TRAUMA (EYR 1)
		NORMAL	11	1-11	NO SIGNIFICANT CLINICAL OBSERVATIONS
1000 PPM		EYES/EARS/NOSE	2	12-13	PROCEDURAL TRAUMA (EYR 2)
	776	NORMAL	11	1-11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
	791	NORMAL	7	1-10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSION SACRIFICE
		BEHAVIOR/CNS	12	2-12	INCOORDINATION
		EYES/EARS/NOSE	1	12	PROCEDURAL TRAUMA (EYL 1)

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
1000 PPM					
791	773	EYES/EARS/NOSE	5	4-10	SWOLLEN PERIOCLULAR TISSUE (EYB 5)
		NORMAL	7	1-10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	13	SCHEDULED SACRIFICE
782		BEHAVIOR/CNS	13	2-12	INCOORDINATION
		EYES/EARS/NOSE	2	12-13	PROCEDURAL TRAUMA (EYL 2)
			1	13	PERINASAL ENCRUSTATION
782		NORMAL	5	1-8	SWOLLEN PERIOCLULAR TISSUE (EYB 1)
		FATE	1	13	NO SIGNIFICANT CLINICAL OBSERVATIONS
		BEHAVIOR/CNS	17	2-13	SCHEDULED SACRIFICE
795		EYES/EARS/NOSE	1	11	INCOORDINATION
			3	12-13	HYPOACTIVE
			1	13	PERINASAL ENCRUSTATION
795		NORMAL	1	13	PERIOCLULAR ENCRUSTATION (EYR 1)
		FATE	1	10	PERIOCLULAR ENCRUSTATION (EYB 1)
		BEHAVIOR/CNS	6	1-9	SWOLLEN PERIOCLULAR TISSUE (EYB 1)
794		NORMAL	1	13	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	14	2-12	SCHEDULED SACRIFICE
		BEHAVIOR/CNS	1	11	INCOORDINATION
786		EYES/EARS/NOSE	1	11	HYPOACTIVE
			1	13	PERIOCLULAR ENCRUSTATION (EYL 1)
			4	9-12	SWOLLEN PERIOCLULAR TISSUE (EYB 2, EYL 2)
767		NORMAL	5	1-8	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSSION SACRIFICE
		BEHAVIOR/CNS	15	2-12	INCOORDINATION
766		EYES/EARS/NOSE	2	9-10	SWOLLEN PERIOCLULAR TISSUE (EYB 2)
			4	1-7	NO SIGNIFICANT CLINICAL OBSERVATIONS
		FATE	1	12	SCHEDULED PERFUSSION SACRIFICE
767		BEHAVIOR/CNS	15	2-12	INCOORDINATION
		EYES/EARS/NOSE	1	12	PROCEDURAL TRAUMA (EYL 1)
			2	9-10	SWOLLEN PERIOCLULAR TISSUE (EYB 2)
765		NORMAL	2	5-8	PERIOCLULAR ENCRUSTATION (EYB 1, EYL 1)
		FATE	7	1-11	NO SIGNIFICANT CLINICAL OBSERVATIONS
		BEHAVIOR/CNS	13	2-12	SCHEDULED PERFUSSION SACRIFICE
768		EYES/EARS/NOSE	1	12	INCOORDINATION
			13	2-12	INCOORDINATION
		FATE	1	10	SWOLLEN PERIOCLULAR TISSUE (EYB 4)
765		NORMAL	4	5-10	PERIOCLULAR ENCRUSTATION (EYB 1)
		FATE	1	9	NO SIGNIFICANT CLINICAL OBSERVATIONS
		BEHAVIOR/CNS	6	1-13	SCHEDULED SACRIFICE
768		EYES/EARS/NOSE	15	2-12	INCOORDINATION
			3	12-13	PERIOCLULAR ENCRUSTATION (EYL 3)
		FATE	2	10-13	SWOLLEN PERIOCLULAR TISSUE (EYB 1, EYL 1)
768		NORMAL	1	12	PROCEDURAL TRAUMA (EYL 1)
		FATE	7	1-10	NO SIGNIFICANT CLINICAL OBSERVATIONS
			1	12	SCHEDULED PERFUSSION SACRIFICE

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CLINICAL OBSERVATIONS
FEMALES

DOSAGE GROUP	ANIMAL	CATEGORY	#	STUDY DAYS	FINDING
1000 PPM					
	768	BEHAVIOR/CNS EYES/EARS/NOSE	13	2- 12	INCOORDINATION
		NORMAL	1	10	SWOLLEN PERIOCLULAR TISSUE (EYB 1)
	787	FATE	6	1- 10	NO SIGNIFICANT CLINICAL OBSERVATIONS
		BEHAVIOR/CNS EYES/EARS/NOSE	15	2- 12	INCOORDINATION
			1	13	SCHEDULED SACRIFICE
			1	13	PERIOCLULAR ENCRUSTATION (EYL 1)
			2	9- 10	SWOLLEN PERIOCLULAR TISSUE (EYB 2)

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

Individual Body Weight Data

(11 Pages)

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TABLE 1

VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL BODY WEIGHT DATA

ABBREVIATIONS

The following is a list of abbreviations or words that may appear in this appendix.

sacr = indicates that the animal was a scheduled sacrifice prior to the period in which this abbreviation appears.

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

DAY	ANIMAL	INDIVIDUAL BODY WEIGHT (GRAMS)					
		MALES GROUP:			0 PPM		
		1	2	5	8	9	12
	717	144.2	147.4	151.1	159.7	164.1	sacr
	735	146.9	151.9	161.0	168.8	173.0	174.4
	752	152.8	156.4	164.3	172.3	175.2	178.7
	715	154.6	157.8	162.6	170.6	175.2	sacr
	711	158.7	162.3	172.5	181.1	186.2	191.7
	750	168.9	175.0	184.6	196.9	201.7	sacr
	751	163.4	166.1	174.4	181.1	186.0	sacr
	706	170.7	176.5	181.6	190.4	193.3	191.9
	738	170.5	176.4	181.7	189.7	194.4	sacr
	728	183.1	185.2	195.3	205.3	210.6	213.6
MEAN		161.4	165.5	172.9	181.6	186.0	190.1
S.D.		12.18	12.39	13.31	14.10	14.35	15.28
N		10	10	10	10	10	5

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

DAY	ANIMAL	INDIVIDUAL BODY WEIGHT (GRAMS)					MALES GROUP:		
		1	2	5	8		9	100 PPM	12
	740	150.6	150.1	159.6	166.9		170.4	176.1	
	714	147.3	149.9	159.7	169.8		173.3	177.6	
	745	156.0	157.6	161.2	168.9		171.7	sacr	
	703	157.4	159.8	168.4	177.9		180.6	sacr	
	725	158.9	161.0	166.0	172.8		175.6	174.4	
	709	159.3	161.8	166.1	173.3		178.5	sacr	
	755	171.1	174.0	182.4	193.7		196.2	sacr	
	716	169.6	171.5	181.8	190.5		193.7	196.1	
	736	172.1	172.7	182.5	190.9		193.0	196.8	
	719	182.3	185.4	195.1	205.6		208.6	sacr	
MEAN		162.4	164.4	172.3	181.0		184.2	184.2	
S.D.		10.93	11.31	12.27	13.16		12.88	11.23	
N		10	10	10	10		10	5	

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

DAY	ANIMAL	INDIVIDUAL BODY WEIGHT (GRAMS)				
		1	2	5	8	MALES GROUP: 500 PPM
						9
						12
	743	147.0	149.5	155.0	161.3	165.2
	757	152.3	156.3	166.1	181.5	186.2
	720	152.0	153.3	160.1	165.9	168.3
	710	157.9	160.7	166.0	172.9	176.9
	731	165.7	171.2	182.2	193.5	198.6
	730	167.8	173.0	178.6	192.4	196.8
	722	162.6	162.8	168.9	178.8	180.6
	721	168.1	169.9	177.1	187.6	190.0
	713	167.2	167.4	178.4	188.4	189.4
	724	183.7	182.4	188.9	201.3	201.8
MEAN		162.4	164.7	172.1	182.4	185.4
S.D.		10.62	10.06	10.61	12.74	12.49
N		10	10	10	10	10
						5
						189.7
						189.7
						191.0
						194.8
						184.5
						15.20
						5

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

DAY	ANIMAL	INDIVIDUAL BODY WEIGHT (GRAMS)					MALES GROUP: 1000 PPM		
		1	2	5	8		9	12	
	733	148.9	150.3	150.9	155.4	157.1	157.1	153.6	sacr
	729	158.3	158.9	157.9	172.7	174.1	174.1	174.1	sacr
	712	156.1	159.4	156.0	164.7	166.7	166.7	166.7	sacr
	727	157.6	159.9	152.0	157.2	145.5	145.5	145.5	sacr
	739	163.6	169.6	173.9	182.2	185.3	185.3	185.3	sacr
	744	166.3	171.5	172.0	178.3	185.7	185.7	185.8	sacr
	737	166.6	172.2	167.1	173.2	175.2	175.2	171.4	sacr
	723	170.0	174.5	175.9	185.2	185.0	185.0	179.8	sacr
	732	171.9	175.5	182.0	187.5	191.2	191.2	186.5	sacr
	746	179.1	183.8	177.2	183.5	186.2	186.2	186.5	sacr
	MEAN	163.8	167.6	166.5	174.0	175.2	175.2	175.4	
	S.D.	8.83	10.07	11.38	11.53	14.80	14.80	13.59	
	N	10	10	10	10	10	10	5	

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

DAY	ANIMAL	INDIVIDUAL BODY WEIGHT (GRAMS)					
		FEMALES GROUP:			0 PPM		
		1	2	5	8	9	12
	800	116.3	118.8	123.7	126.6	124.3	sacr
	764	119.5	122.5	123.5	131.4	132.4	129.2
	803	122.3	125.4	127.8	131.3	134.4	132.4
	801	119.8	126.6	129.8	132.3	135.8	sacr
	784	128.1	126.8	132.9	134.1	140.7	139.4
	783	122.8	125.0	128.7	134.2	136.5	130.1
	778	130.0	131.3	135.7	135.8	140.2	141.3
	777	126.2	129.4	127.4	135.6	137.8	sacr
	775	128.5	129.6	130.4	136.0	137.3	sacr
	809	139.3	141.5	143.3	145.1	145.7	sacr
MEAN		125.3	127.7	130.3	134.2	136.5	134.5
S.D.		6.65	6.05	5.89	4.76	5.68	5.52
N		10	10	10	10	10	5

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

DAY	ANIMAL	INDIVIDUAL BODY WEIGHT (GRAMS)					FEMALES GROUP: 100 PPM		
		1	2	5	8	9	12		
	797	114.9	118.7	120.1	129.5	131.0	sacr		
	810	115.1	120.5	123.5	129.5	129.6	sacr		
	793	116.9	121.9	124.5	128.7	130.5	128.9		
	789	125.2	127.9	134.4	137.1	143.9	140.4		
	780	123.2	124.2	130.5	132.3	137.6	136.0		
	779	123.1	130.8	132.9	139.6	140.2	141.1		
	807	130.2	133.9	135.7	141.4	140.6	sacr		
	785	137.9	138.9	144.7	147.9	151.0	sacr		
	772	132.3	131.6	136.5	142.1	146.0	139.5		
	799	138.8	141.1	143.4	150.9	151.9	sacr		
MEAN		125.8	129.0	132.6	137.9	140.2	137.2		
S.D.		8.82	7.68	8.17	7.88	8.15	5.04		
N		10	10	10	10	10	5		

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

DAY	ANIMAL	INDIVIDUAL BODY WEIGHT (GRAMS)				
		1	2	5	8	9
		FEMALES GROUP: 500 PPM				
						12
	770	120.6	119.1	123.4	126.5	126.5
	805	127.2	128.0	134.6	140.1	138.9
	788	123.2	123.2	124.2	128.0	131.5
	806	125.7	126.8	131.0	132.9	132.0
	808	121.9	124.9	127.6	129.9	134.2
	762	123.6	120.7	122.7	124.9	122.7
	781	131.5	129.7	132.1	135.6	138.4
	771	130.0	130.6	133.1	139.5	139.4
	774	130.0	131.1	130.0	131.5	128.9
	776	135.2	136.2	136.9	139.9	136.9
	MEAN	126.9	127.0	129.6	132.9	133.0
	S.D.	4.73	5.21	4.94	5.68	5.67
	N	10	10	10	10	10
						5

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

DAY	ANIMAL	INDIVIDUAL BODY WEIGHT (GRAMS)					FEMALES GROUP: 1000 PPM		
		1	2	5	8	9	12	12	12
	791	113.8	118.0	112.5	114.7	114.5	sacr		
	773	112.9	118.0	115.6	119.5	118.9	120.1		
	782	121.6	122.4	120.2	121.6	121.7	119.8		
	795	124.0	128.5	126.3	125.9	128.7	126.0		
	794	133.9	133.2	125.8	129.3	131.9	sacr		
	786	127.7	126.3	124.2	124.5	127.3	sacr		
	767	123.2	129.4	120.6	122.5	123.2	sacr		
	765	128.3	131.9	126.8	130.6	132.8	126.7		
	768	128.7	130.2	129.4	129.6	131.7	sacr		
	787	137.1	138.1	133.9	137.5	139.6	135.9		
MEAN		125.1	127.6	123.5	125.6	127.0	125.7		
S.D.		7.80	6.54	6.40	6.50	7.50	6.51		
N		10	10	10	10	10	5		

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats
Individual Food Consumption Data
(11 Pages)

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TABLE 1
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMPTION DATA

ABBREVIATIONS

The following is a list of abbreviations or words that may appear in this appendix.

r/s = indicates that the animal was removed from the consumption period due to spillage.

r/e = indicates that the animal was removed from the consumption period due to excreta in the feeder

r/o = indicates that the animal was removed from the consumption period for reasons specified in the raw data.

r/dead = indicates that the animal was removed from the consumption period because it died or was sacrificed during the period in which this abbreviation appears.

sacr = indicates that the animal was a scheduled sacrifice prior to the period in which this abbreviation appears.

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

DAY	ANIMAL	INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)		
		MALES GROUP: 0 PPM		
		5	8	10
	717	14.0	15.2	13.5
	735	14.2	15.3	13.8
	752	14.6	15.3	13.6
	715	13.5	15.3	13.4
	711	14.8	16.7	15.3
	750	17.0	18.9	16.2
	751	14.9	16.7	14.7
	706	16.2	17.7	15.3
	738	15.4	17.0	14.6
	728	16.7	18.3	16.7
MEAN		15.1	16.6	14.7
S.D.		1.17	1.34	1.16
N		10	10	10

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
MALES GROUP: 100 PPM

DAY	5	8	10
ANIMAL			
740	13.6	15.6	13.9
714	13.4	16.0	12.9
745	14.2	16.2	12.8
703	14.1	16.5	13.3
725	14.2	15.7	13.1
709	12.7	15.0	12.6
755	15.9	18.8	14.9
716	15.2	18.0	14.1
736	15.8	17.3	15.2
719	17.1	19.0	16.1
MEAN	14.6	16.8	13.9
S.D.	1.33	1.39	1.18
N	10	10	10

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
MALES GROUP: 500 PPM

DAY	5	8	10
ANIMAL			
743	13.2	17.3	12.5
757	14.4	17.4	14.8
720	13.8	16.1	12.7
710	14.5	16.6	13.1
731	15.7	18.8	15.5
730	14.4	17.6	12.8
722	13.4	15.7	13.3
721	14.5	16.7	13.0
713	14.4	18.0	13.0
724	15.4	19.5	14.6
MEAN	14.4	17.4	13.5
S.D.	0.78	1.19	1.05
N	10	10	10

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

MALES GROUP: 1000 PPM

DAY	5	8	10
ANIMAL			
733	9.5	14.3	9.6
729	10.5	18.5	12.9
712	9.9	16.3	8.3
727	9.9	14.9	9.3
739	11.6	18.4	11.4
744	11.7	18.5	13.6
737	9.8	16.8	9.3
723	10.9	19.1	10.4
732	12.0	17.3	13.3
746	11.6	17.0	12.9
MEAN	10.7	17.1	11.1
S.D.	0.93	1.59	1.97
N	10	10	10

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

DAY	ANIMAL	INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)		
		FEMALES GROUP: 0 PPM		
		5	8	10
	800	10.9	12.2	11.1
	764	10.7	12.4	10.2
	803	11.1	11.3	10.9
	801	11.0	10.9	11.8
	784	11.3	11.3	12.5
	783	11.4	11.7	12.2
	778	11.4	11.4	12.0
	777	10.5	12.1	11.0
	775	11.3	12.2	10.7
	809	10.9	12.1	12.1
MEAN		11.1	11.8	11.4
S.D.		0.30	0.50	0.77
N		10	10	10

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)

FEMALES GROUP: 100 PPM

DAY	5	8	10
ANIMAL			
797	10.3	13.5	11.2
810	11.5	13.8	10.2
793	10.4	12.5	11.0
789	11.3	12.5	12.2
780	10.9	13.0	12.3
779	10.6	13.0	11.0
807	11.3	13.7	11.5
785	12.2	14.3	12.7
772	10.2	11.7	12.4
799	11.3	13.7	11.9
MEAN	11.0	13.2	11.6
S.D.	0.63	0.77	0.79
N	10	10	10

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
FEMALES GROUP: 500 PPM

DAY	5	8	10
ANIMAL			
770	9.7	12.1	10.2
805	12.0	15.0	11.4
788	10.4	12.0	11.0
806	10.6	12.5	11.2
808	10.4	11.9	10.9
762	7.7	11.7	8.8
781	10.3	11.9	12.4
771	9.6	12.9	10.5
774	10.1	11.8	9.9
776	10.0	12.1	9.9
MEAN	10.1	12.4	10.6
S.D.	1.07	0.99	0.98
N	10	10	10

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FOOD CONSUMPTION (GRAMS/ANIMAL/DAY)
FEMALES GROUP: 1000 PPM

DAY	5	8	10
ANIMAL			
791	8.6	12.3	9.2
773	9.4	12.3	9.9
782	9.6	11.8	8.3
795	9.8	11.4	8.8
794	9.2	13.0	9.4
786	8.7	12.4	8.9
767	8.9	11.8	10.0
765	9.6	12.9	8.6
768	10.4	11.3	8.1
787	9.0	13.3	9.8
MEAN	9.3	12.2	9.1
S.D.	0.56	0.66	0.67
N	10	10	10

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats
Functional Observational Battery Individual Data and Information
(38 Pages)

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Note: Units of measurements for the following are:

Grip Strength - Kilograms (kg)
Body Temperature - Degrees Celsius (°C)
Body Weight - Grams (g)
Hind Leg Splay - Centimeters (cm)

TABLE 1
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

FUNCTIONAL OBSERVATIONAL BATTERY INDIVIDUAL DATA

ABBREVIATIONS

The following is a list of abbreviations or words that may appear in this appendix.

<u>Parameter</u>	<u>Abbreviation</u>	<u>Corresponding Name</u>
Cage Posture	NormAwake	Normal/awake
	NormAslee	Normal/asleep
	SideProst	On side/prostrate
	StomProst	On stomach/prostrate
Handling Reactivity	Resists	Slight/moderate resistance
	Limp	Animal limp
	HighResis	High resistance/aggressive
Gait	Uncoord	Uncoordinated
	Splayed	Limbs exaggerated/splayed
	OnToes	Walks on toes
Body Position	OnSide	On side
	OnStomach	On stomach
Breathing Pattern	Mthbreath	Mouthbreathing
	Rapid	Rapid respiration
Clonic Convulsions	RunFits	Running fits
(cageside and open field)	ExplJumps	Explosive jumps
Tremor or Jerk	WholeBody	Whole body
(cageside and open field)		
Unusual Behavior	Retropuls	Retropulsion
	HeadBob	Head bobbing/weaving
	Stereotyp	Stereotypy
	Active	Active/alert
Arousal	Hyperact	Hyperactive/hyperalert
	InacAlert	Inactive/alert
	NotAlert	Inactive/not alert
	WideOpen	Wide open
Palpebral Closure	SlDroop	Slightly drooping
	HalfShut	Halfway shut
	Shut	Completely shut
	None	No reaction
Approach, Startle, and Tail Pinch Responses	Noticable	Noticeable reaction
	Exagger	Exaggerated reaction
Fur Appearance	UrinStain	Urine stains/wetness
Additional Observations	Emaciated	Emaciation
	Dehydrat	Dehydration
	Exophthal	Exophthalmus
	FeetCoord	Feet/coordinated
Air Righting	FeetUncoord	Feet/uncoordinated

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
PREEXPOSURE

OBSERVATION	MALES GROUP:0 PPM									
	ANIMAL NUMBERS									
	717	735	752	715	711	750	751	706	738	728
Cage Posture	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee
Cage Palpebral Closure	Shut	Shut	HalfShut	Shut	WideOpen	Shut	Shut	SLDroop	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

OBSERVATION	MALES GROUP:100 PPM									
	ANIMAL NUMBERS									
	740	714	745	703	725	709	755	716	736	719
Cage Posture	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee
Cage Palpebral Closure	Shut	HalfShut	Shut	WideOpen	WideOpen	Shut	WideOpen	HalfShut	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
PREEXPOSURE

OBSERVATION	MALES GROUP:500 PPM									
	ANIMAL NUMBERS									
	743	757	720	710	731	730	722	721	713	724
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	Shut	HalfShut	Shut	HalfShut
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

OBSERVATION	MALES GROUP:1000 PPM									
	ANIMAL NUMBERS									
	733	729	712	727	739	744	737	723	732	746
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	HalfShut	WideOpen	Shut	Shut	Shut	SlDroop	Shut	Shut	WideOpen
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

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TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
PREEXPOSURE

OBSERVATION	MALES GROUP:0 PPM										ANIMAL NUMBERS			
	717	735	752	715	711	750	751	706	738	728				
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists				
Ataxia	No	No	No	No	No	No	No	No	No	No				
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal				
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal				
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None				
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal				
Twitch	None	None	None	None	None	None	None	None	None	None				
Tremor	None	None	None	None	None	None	None	None	None	None				
Spasm	None	None	None	None	None	None	None	None	None	None				
Jerk	None	None	None	None	None	None	None	None	None	None				
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None				
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None				
Unusual Behavior	None	None	None	None	None	None	None	None	None	None				
Arousal	Active	Active	Active	Active	Active	Active	Active	Active	Active	Active				
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen				
Defecation	Normal	None	None	None	None	None	None	None	None	None				
Urine	Present	None	None	Present	None	None	None	None	Present	None				
Piloerection	None	None	None	None	None	None	None	None	None	None				
Rears	11	13	25	3	20	21	26	6	8	8				
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable				
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable				
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable				
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal				
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal				
Lacrimation	None	None	None	None	None	None	None	None	None	None				
Salivation	None	None	None	None	None	None	None	None	None	None				
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal				
Facial Crust	None	None	None	None	None	None	None	None	None	None				
Additional Observations	None	None	None	None	None	None	None	None	None	None				
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present				
Grip Strength #1 (fore)	.49	.52	.41	.51	.70	.56	.61	.49	.62	.58				
Grip Strength #2 (fore)	.40	.61	.40	.62	.65	.53	.54	.46	.43	.65				
Grip Strength #1 (hind)	.33	.33	.26	.25	.31	.32	.30	.25	.35	.33				
Grip Strength #2 (hind)	.29	.26	.24	.29	.35	.35	.31	.21	.25	.25				
Body Temperature	38.10	38.00	38.10	38.00	37.70	38.00	38.70	38.20	38.00	37.70				
Body Weight	130.14	133.50	135.26	139.62	139.70	146.66	145.62	150.00	153.18	158.26				
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord				
Hind Leg Splay #1	2.90	3.40	2.60	5.90	5.00	4.70	4.10	3.80	4.30	3.10				
Hind Leg Splay #2	2.90	3.20	2.20	6.30	4.50	4.80	4.20	4.30	3.20	3.90				

TABLE 3
VINYL PIVALATE; TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
PREEXPOSURE

MALES GROUP:100 PPM

OBSERVATION	ANIMAL NUMBERS									
	740	714	745	703	725	709	755	716	736	719
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None	None	None	None	None
Urine	None	None	None	None	None	None	None	None	None	None
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	24	15	17	9	8	9	13	4	12	9
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Visual Placing	.40	.52	.51	.47	.43	.64	.40	.63	.49	.47
Grip Strength #1 (fore)	.43	.63	.49	.52	.46	.65	.37	.60	.51	.44
Grip Strength #2 (fore)	.25	.27	.25	.22	.22	.36	.28	.33	.26	.30
Grip Strength #1 (hind)	.18	.27	.27	.27	.18	.38	.27	.30	.26	.21
Grip Strength #2 (hind)	38.20	37.80	38.00	37.80	38.00	37.90	38.10	38.20	38.00	38.20
Body Temperature	132.70	130.80	139.38	138.40	141.96	142.84	148.48	146.74	153.86	159.98
Body Weight	FootCoord	FootCoord	FootCoord	FootCoord	FootCoord	FootCoord	FootCoord	FootCoord	FootCoord	FootCoord
Air Weighting	3.80	3.30	4.40	4.20	4.70	2.50	3.30	4.50	4.20	3.80
Hind Leg Splay #1	4.50	4.00	5.50	3.10	3.20	3.50	3.80	4.30	3.40	3.50
Hind Leg Splay #2										

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
PREEXPOSURE

MALES GROUP:500 PPM

OBSERVATION	ANIMAL NUMBERS									
	743	757	720	710	731	730	722	721	713	724
Handling Reactivity	Resists No	Resists No	Resists No	Resists No	Resists No	Resists No	Resists No	Resists No	Resists No	Resists No
Ataxia	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Urine	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	7	13	7	11	10	5	17	11	19	22
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.49	.60	.58	.44	.47	.55	.52	.39	.69	.70
Grip Strength #2 (fore)	.43	.49	.55	.41	.48	.44	.56	.35	.58	.58
Grip Strength #1 (hind)	.33	.37	.30	.24	.27	.36	.35	.27	.22	.37
Grip Strength #2 (hind)	.30	.35	.30	.20	.35	.33	.30	.17	.21	.40
Body Temperature	38.10	38.10	38.30	37.50	37.80	38.40	38.10	37.70	38.20	38.00
Body Weight	131.08	134.04	136.44	140.46	143.66	150.16	142.20	150.28	150.50	158.56
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
M.H.3 Lev 54.4, 01	1.00	5.00	2.40	2.60	4.00	2.70	3.50	2.40	8.00	4.30
M.H.3 Lev 54.4, 02	4.10	5.00	2.10	3.50	4.60	3.70	3.30	3.20	4.70	4.00

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
PREEXPOSURE

OBSERVATION	MALES GROUP:1000 PPM									
	733	729	712	727	739	744	737	723	732	746
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	Normal	None	None	None	Normal	None	None	None
Urine	None	None	Present	None	None	None	Present	None	None	None
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	19	16	1	16	15	19	10	12	22	15
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Salivation	None	None	None	None	None	None	None	None	None	None
Lacrimation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.58	.58	.55	.70	.54	.35	.33	.45	.62	.67
Grip Strength #2 (fore)	.51	.58	.52	.61	.54	.40	.35	.48	.55	.66
Grip Strength #1 (hind)	.20	.20	.28	.32	.14	.25	.31	.27	.35	.37
Grip Strength #2 (hind)	.26	.37	.25	.28	.17	.21	.25	.31	.33	.37
Body Temperature	37.90	38.10	39.00	38.00	38.30	37.80	38.20	37.80	37.90	38.50
Body Weight	134.12	136.88	138.76	140.70	141.86	144.02	144.36	150.02	149.22	156.40
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Mind Leg Splay #1	5.30	3.40	3.70	3.70	5.60	3.70	4.30	4.10	4.60	3.40
Mind Leg Splay #2	3.40	3.80	3.20	4.10	4.50	3.70	4.00	4.40	4.70	3.40

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS

DAY 10

MALES GROUP:0 PPM

OBSERVATION	717	735	752	715	711	750	751	706	738	728
	ANIMAL NUMBERS									
Cage Posture	NormAwake	NormAslee	NormAwake	NormAwake	NormAslee	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	Shut	WideOpen	WideOpen	Shut	WideOpen	HalfShut	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

MALES GROUP:100 PPM

OBSERVATION	740	714	745	703	725	709	755	716	736	719
	ANIMAL NUMBERS									
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAslee	NormAslee	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	Sidroop	WideOpen	Sidroop	HalfShut	Shut	Shut	Sidroop	WideOpen	HalfShut	Sidroop
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 10

MALES GROUP: 500 PPM

OBSERVATION	ANIMAL NUMBERS									
	743	757	720	710	731	730	722	721	713	724
Cage Posture	NormAwake	NormAwake	NormAwake	NormAslee	NormAwake	NormAwake	NormAslee	NormAslee	NormAwake	NormAslee
Cage Palpebral Closure	WideOpen	WideOpen	HalfShut	Shut	HalfShut	WideOpen	Shut	Shut	SlDroop	Shut
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

MALES GROUP: 1000 PPM

OBSERVATION	ANIMAL NUMBERS									
	733	729	712	727	739	744	737	723	732	746
Cage Posture	NormAwake	NormAwake	NormAwake	NormAslee	NormAwake	NormAslee	NormAslee	NormAslee	NormAslee	NormAslee
Cage Palpebral Closure	WideOpen	HalfShut	WideOpen	Shut	WideOpen	Shut	Shut	Shut	Shut	Shut
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

RPT_NT:VPTRMCF2.IFO

TABLE 5
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 10

OBSERVATION	MALES GROUP:0 PPM									
	717	735	752	715	711	750	751	706	738	728
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	Active	Active	Inactive	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None	None	None	None	None
Urine	None	None	None	None	None	None	None	None	None	None
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	8	6	11	2	6	10	4	8	16	8
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.61	.58	.63	.65	.71	.71	.68	.77	.53	.76
Grip Strength #2 (fore)	.52	.58	.70	.65	.80	.80	.74	.78	.70	.64
Grip Strength #1 (hind)	.38	.35	.39	.25	.43	.46	.46	.42	.43	.42
Grip Strength #2 (hind)	.39	.33	.40	.23	.46	.48	.40	.38	.40	.38
Body Temperature	38.30	37.60	38.60	38.40	37.60	38.20	37.60	38.30	38.10	38.30
Body Weight	164.62	173.36	173.12	174.20	185.38	204.76	184.82	194.94	192.98	208.30
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	5.50	3.70	4.40	2.80	4.50	3.40	4.80	3.60	2.90	5.50
Hind Leg Splay #2	5.60	5.70	3.50	4.10	4.80	4.50	4.40	4.00	5.30	5.50

TABLE 5
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 10

OBSERVATION	MALES GROUP:100 PPM									
	ANIMAL NUMBERS									
	740	714	745	703	725	709	755	716	736	719
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No	No	No	No	No
Gait	Normal	Uncoord Present	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	Other ^a	None	None	None	None	None	None	None	None
Arousal	Active	InacAlert	InacAlert	Active	Active	Active	InacAlert	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	SLDroop	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None	None	None	None	None
Urine	None	Present	None	None	None	None	None	None	None	None
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	12	0	1	13	12	16	1	3	19	11
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.59	.72	.60	.69	.63	.61	.61	.52	.72	.94
Grip Strength #2 (fore)	.63	.74	.56	.66	.60	.64	.62	.57	.66	.92
Grip Strength #1 (hind)	.39	.41	.23	.29	.32	.25	.37	.42	.40	.36
Grip Strength #2 (hind)	.35	.35	.22	.35	.26	.23	.38	.43	.42	.35
Body Temperature	38.10	37.80	37.50	38.30	38.60	37.80	38.70	37.30	38.30	38.10
Body Weight	172.62	172.86	171.40	178.26	173.94	176.00	195.80	193.18	193.90	208.10
Air Weighting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay, °	1.60	4.00	4.60	3.20	4.10	3.90	4.50	2.70	3.10	4.10
Hind Leg Splay, °	4.70	5.00	5.00	4.80	4.70	4.40	4.60	4.30	3.20	4.80

^aContinuous slight head tilt to the left while in arena

TABLE 5
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 10

MALES GROUP: 500 PPM

OBSERVATION	ANIMAL NUMBERS									
	743	757	720	730	722	721	713	724		
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists		
Ataxia	NO	NO	NO	NO	NO	NO	NO	NO		
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal		
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal		
Excessive Vocalization	None	None	None	None	None	None	None	None		
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal		
Twitch	None	None	None	None	None	None	None	None		
Tremor	None	None	None	None	None	None	None	None		
Spasm	None	None	None	None	None	None	None	None		
Jerk	None	None	None	None	None	None	None	None		
Clonic Convulsions	None	None	None	None	None	None	None	None		
Tonic Convulsions	None	None	None	None	None	None	None	None		
Unusual Behavior	None	None	None	None	None	None	None	None		
Arousal	Active	Active	Active	Active	Active	Active	Active	Active		
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen		
Defecation	None	None	None	None	None	None	None	None		
Urine	None	None	None	None	None	None	None	None		
Piloerection	None	None	None	None	None	None	None	None		
Rears	24	10	4	31	17	2	14	3		
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable		
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable		
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable		
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal		
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal		
Lacrimation	None	None	None	None	None	None	None	None		
Salivation	None	None	None	None	None	None	None	None		
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal		
Facial Crust	None	None	None	None	None	None	None	None		
Additional Observations	None	None	None	None	None	None	None	None		
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present		
Grip Strength #1 (fore)	.77	.44	.47	.63	.75	.89	.48	.61		
Grip Strength #2 (fore)	.69	.46	.46	.78	.83	.63	.50	.70		
Grip Strength #1 (hind)	.44	.30	.38	.37	.36	.48	.41	.36		
Grip Strength #2 (hind)	.39	.25	.38	.36	.33	.42	.38	.34		
Body Temperature	38.50	38.00	37.90	38.50	38.50	38.70	37.30	38.00		
Body Weight	163.06	185.44	169.32	174.42	196.38	195.44	177.74	190.60		
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord		
Mind Leg Splay #1	4.50	5.50	2.50	4.10	4.40	5.30	3.20	6.60		
Mind Leg Splay #2	4.50	5.50	3.20	3.70	5.50	4.20	4.70	4.30		

TABLE 5
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS

DAY 10

MALES GROUP:1000 PPM

OBSERVATION	ANIMAL NUMBERS									
	733	729	712	727	739	744	737	723	732	746
Handling Reactivity	Resists No	Resists No	Resists No	Resists No	Resists No	Resists No	Resists Yes	Resists No	Resists No	Resists No
Ataxia							Present			
Gait	Normal	Uncoord Present	Uncoord Present	Uncoord Present	Uncoord Present	Uncoord Present	Uncoord Present	Uncoord Present	Uncoord Present	Uncoord Present
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	InacAlert	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	SlDrop	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	Normal	None	None	None	None
Urine	None	None	None	None	None	None	None	None	None	None
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	6	10	4	8	7	0	8	3	9	7
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Decreased	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.41	.43	.42	.61	.71	.38	.37	.55	.55	.59
Grip Strength #2 (fore)	.47	.42	.48	.63	.76	.45	.46	.51	.49	.47
Grip Strength #1 (hind)	.37	.30	.37	.37	.38	.38	.40	.33	.27	.38
Grip Strength #2 (hind)	.30	.29	.39	.25	.35	.35	.38	.31	.30	.36
Body Temperature	37.70	38.00	38.50	37.60	38.20	37.40	37.40	37.60	38.10	37.70
Body Weight	156.46	175.40	164.06	158.84	182.90	185.20	174.04	183.52	187.32	188.72
Air Righting	FeetCoord	FeetCoord	FeetCoord	Back	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	5.70	7.20	10.40	6.90	8.10	7.40	7.70	5.80	8.30	8.80
Hind Leg Splay #2	7.00	7.40	9.70	7.80	8.10	6.60	10.20	5.50	8.20	7.70

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
PREEXPOSURE

FEMALES GROUP:0 PPM

OBSERVATION	800	764	803	801	784	783	778	777	775	809
	ANIMAL NUMBERS									
Cage Posture	NormAwake	NormAslee	NormAslee	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	Shut	Shut	HalfShut	Shut	HalfShut	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

FEMALES GROUP:100 PPM

OBSERVATION	797	810	793	789	780	779	807	785	772	799
	ANIMAL NUMBERS									
Cage Posture	NormAslee	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAslee	NormAwake	NormAwake	NormAslee
Cage Palpebral Closure	Shut	HalfShut	HalfShut	WideOpen	WideOpen	HalfShut	Shut	WideOpen	WideOpen	Shut
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
PREEXPOSURE

FEMALES GROUP: 500 PPM

OBSERVATION	770	805	788	806	808	762	781	771	774	776
Cage Posture	NormAwake	NormAslee	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAslee	NormAwake
Cage Palpebral Closure	HalfShut	Shut	WideOpen	WideOpen	WideOpen	WideOpen	HalfShut	Sidroop	Shut	HalfShut
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

FEMALES GROUP: 1000 PPM

OBSERVATION	791	773	782	795	794	786	767	765	768	787
Cage Posture	NormAwake	NormAwake	NormAwake	NormAslee	NormAslee	NormAwake	NormAwake	NormAwake	NormAslee	NormAslee
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	Shut	Shut	WideOpen	HalfShut	WideOpen	Shut	Shut
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

RPT_NT:VPTRFCFL.IFO

TABLE 7
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
PREEXPOSURE

FEMALES GROUP:0 PPM

OBSERVATION	ANIMAL NUMBERS									
	800	764	803	801	784	783	778	777	775	809
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active	Inactive	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None	None	None	None	None
Urine	Present	None	None	None	None	Present	None	None	Present	Present
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	20	12	21	19	22	4	1	7	16	21
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.48	.57	.62	.50	.50	.43	.76	.46	.47	.66
Grip Strength #2 (fore)	.40	.53	.58	.49	.51	.47	.76	.61	.57	.62
Grip Strength #1 (hind)	.26	.25	.22	.31	.22	.21	.22	.30	.23	.33
Grip Strength #2 (hind)	.18	.23	.21	.33	.23	.25	.27	.26	.23	.25
Body Temperature	37.80	37.50	37.70	37.80	38.10	38.00	38.60	37.60	37.80	37.20
Body Weight	109.42	111.78	117.00	118.93	123.24	119.10	125.74	125.24	125.70	134.06
Air Weighting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	3.10	4.10	4.10	3.50	4.10	3.10	2.20	3.50	2.00	2.50
Hind Leg Splay #2	3.70	4.00	5.10	3.20	4.20	3.50	2.40	3.40	2.70	3.20

TABLE 7
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
PREEXPOSURE

FEMALES GROUP:100 PPM

OBSERVATION	ANIMAL NUMBERS									
	797	810	793	789	780	779	807	785	772	799
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None	None	None	None	None
Urine	Present	None	None	None	Present	None	None	None	None	None
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	15	17	11	21	21	16	11	25	16	18
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.42	.52	.58	.57	.61	.60	.49	.45	.45	.56
Grip Strength #2 (fore)	.47	.42	.63	.63	.68	.53	.45	.45	.49	.63
Grip Strength #1 (hind)	.21	.26	.28	.32	.26	.33	.33	.35	.33	.42
Grip Strength #2 (hind)	.23	.32	.33	.30	.26	.36	.31	.27	.33	.39
Body Temperature	37.60	38.10	38.40	38.10	37.70	37.60	37.80	38.10	37.90	37.70
Body Weight	108.90	114.66	116.44	119.28	118.48	124.88	123.88	130.58	127.78	133.08
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.80	2.90	2.70	3.30	3.70	3.10	4.30	2.50	3.10	3.80
Hind Leg Splay #2	3.50	3.50	3.10	3.50	3.80	3.90	2.80	3.50	3.00	4.20

TABLE 7
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
PREEXPOSURE

FEMALES GROUP: 500 PPM

OBSERVATION	770	805	788	806	808	762	781	771	774	776
	ANIMAL NUMBERS									
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None	None	None	None	None
Urine	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	19	18	20	23	30	13	11	13	28	16
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Exagger	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.38	.50	.61	.48	.51	.40	.59	.49	.46	.52
Grip Strength #2 (fore)	.43	.54	.55	.51	.58	.36	.52	.46	.57	.60
Grip Strength #1 (hind)	.29	.20	.32	.27	.30	.32	.22	.26	.37	.41
Grip Strength #2 (hind)	.28	.23	.34	.28	.29	.36	.25	.25	.30	.29
Body Temperature	37.90	38.00	37.70	38.10	37.60	37.80	37.50	37.60	38.30	37.60
Body Weight	110.20	117.58	115.54	114.16	117.78	119.14	124.06	126.26	124.36	124.96
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	3.00	4.00	5.50	3.50	2.00	3.40	4.30	3.00	2.90	3.50
Hind Leg Splay #2	4.10	3.80	3.90	4.30	2.40	3.90	3.30	3.80	3.10	4.10

TABLE 7
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
PREEXPOSURE

FEMALES GROUP:1000 PPM

OBSERVATION	ANIMAL NUMBERS									
	791	773	782	795	794	786	767	765	768	787
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None	None	None	None	None
Urine	Present	Present	None	None	None	Present	None	None	Present	Present
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	12	19	7	15	23	14	10	21	12	18
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.71	.47	.65	.56	.58	.62	.51	.68	.65	.64
Grip Strength #2 (fore)	.51	.39	.52	.51	.50	.65	.52	.59	.69	.50
Grip Strength #1 (hind)	.17	.28	.39	.28	.31	.25	.35	.36	.26	.41
Grip Strength #2 (hind)	.16	.22	.35	.28	.30	.26	.30	.37	.30	.38
Body Temperature	38.10	37.70	37.50	37.60	37.70	38.10	38.00	37.70	37.50	37.60
Body Weight	112.14	111.56	117.66	118.18	121.72	121.46	123.88	126.42	127.08	130.86
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	3.00	1.90	3.90	3.50	4.20	2.80	3.00	2.40	3.50	2.80
Hind Leg Splay #2	3.00	2.90	3.30	3.50	3.90	3.20	2.50	2.00	3.00	3.00

RPT_NT:VPTREF1.IFO

01/27/95

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS
DAY 11

FEMALES GROUP:0 PPM

OBSERVATION	ANIMAL NUMBERS									
	800	764	803	801	784	783	778	777	775	809
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

FEMALES GROUP:100 PPM

OBSERVATION	ANIMAL NUMBERS									
	797	810	793	789	780	779	807	785	772	799
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL CAGESIDE FUNCTIONAL OBSERVATIONS

DAY 11

FEMALES GROUP:500 PPM

OBSERVATION	770	805	788	806	808	762	781	771	774	776
	ANIMAL NUMBERS									
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	HalfShut	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

FEMALES GROUP:1000 PPM

OBSERVATION	791	773	782	795	794	786	767	765	768	787
	ANIMAL NUMBERS									
Cage Posture	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake	NormAwake
Cage Palpebral Closure	SidRoop	HalfShut	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	HalfShut	WideOpen
Cage Twitch	None	None	None	None	None	None	None	None	None	None
Cage Tremor	None	None	None	None	None	None	None	None	None	None
Cage Spasm	None	None	None	None	None	None	None	None	None	None
Cage Jerk	None	None	None	None	None	None	None	None	None	None
Cage Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Cage Tonic Convulsions	None	None	None	None	None	None	None	None	None	None

RPT_NT:VPTRECF2.IFO

TABLE 9
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 11

FEMALES GROUP:0 PPM

OBSERVATION	800	764	803	801	784	783	778	777	775	809
	ANIMAL NUMBERS									
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	InacAlert	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	SLDroop	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	Present	None	None	None	None
Urine	None	None	None	None	None	Present	None	None	None	Present
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	15	18	8	4	13	4	8	23	26	12
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.50	.64	.53	.73	.55	.55	.73	.65	.59	.79
Grip Strength #2 (fore)	.46	.67	.53	.70	.56	.58	.69	.71	.75	.62
Grip Strength #1 (hind)	.23	.33	.34	.40	.25	.36	.40	.29	.43	.42
Grip Strength #2 (hind)	.26	.32	.35	.41	.24	.43	.40	.27	.35	.36
Body Temperature	38.20	37.70	37.60	38.10	38.10	37.30	38.10	39.00	38.30	37.80
Body Weight	129.98	131.30	135.26	134.16	140.68	133.64	142.56	140.40	139.44	146.90
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Mind Leg Splay #1	2.20	3.10	4.40	2.80	3.30	4.30	3.00	4.10	3.60	3.80
Mind Leg Splay #2	3.60	3.20	4.50	4.00	3.30	2.90	3.40	3.00	3.70	3.60

TABLE 9
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 11

FEMALES GROUP:100 PPM

OBSERVATION	797	810	793	789	780	779	807	785	772	799
	ANIMAL NUMBERS									
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	InacAlert	InacAlert	Active	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None	None	None	None	None
Urine	None	None	None	None	None	None	None	None	None	None
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	14	1	1	7	12	26	11	19	14	17
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.65	.31	.72	.71	.60	.56	.59	.68	.43	.56
Grip Strength #2 (fore)	.61	.32	.59	.66	.53	.59	.59	.59	.49	.67
Grip Strength #1 (hind)	.35	.29	.38	.31	.25	.38	.36	.40	.34	.42
Grip Strength #2 (hind)	.32	.23	.35	.30	.27	.46	.36	.41	.30	.34
Body Temperature	38.00	38.30	38.10	38.00	38.30	39.30	38.40	38.40	37.80	38.70
Body Weight	131.84	132.40	132.52	142.90	140.34	139.12	144.02	153.04	146.46	150.66
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	3.00	2.20	2.10	3.00	2.70	2.40	2.50	3.30	2.40	3.90
Hind Leg Splay #2	3.40	3.80	3.70	4.10	3.10	4.00	3.50	3.90	4.00	4.20

*Right pupil size was increased while the left pupil size was normal

TABLE 9
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 11

FEMALES GROUP:500 PPM

OBSERVATION	ANIMAL NUMBERS									
	770	805	788	806	808	762	781	771	774	776
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	No	No	No	No	No	No	No	No	No
Gait	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Body Position	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Excessive Vocalization	None	None	None	None	None	None	None	None	None	None
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerk	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	Active	Active	Active	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None	None	None	None	None
Urine	None	None	None	None	None	None	None	None	None	None
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	18	6	21	15	26	6	6	8	31	21
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.61	.58	.50	.74	.42	.62	.39	.69	.67	.54
Grip Strength #2 (fore)	.56	.61	.53	.64	.47	.55	.44	.70	.55	.50
Grip Strength #1 (hind)	.34	.30	.33	.39	.33	.33	.25	.38	.34	.32
Grip Strength #2 (hind)	.31	.27	.30	.40	.33	.36	.27	.33	.34	.40
Body Temperature	37.70	38.20	38.20	38.60	38.30	38.60	37.90	37.50	38.30	37.70
Body Weight	128.40	140.22	129.46	137.00	133.48	127.70	135.56	141.62	136.56	141.32
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	Side	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	4.20	4.80	4.70	5.50	2.70	3.40	2.60	3.50	5.20	3.90
Hind Leg Splay #2	4.50	6.20	3.80	4.00	2.70	3.00	2.50	2.90	3.70	4.10

TABLE 9
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL FUNCTIONAL OBSERVATIONS
DAY 11

FEMALES GROUP:1000 PPM

OBSERVATION	ANIMAL NUMBERS									
	791	773	782	795	794	786	767	765	768	787
Handling Reactivity	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists	Resists
Ataxia	No	Yes	No	No	No	No	No	No	No	No
Gait	Uncoord	Uncoord	Uncoord	Uncoord	Uncoord	Uncoord	Uncoord	Uncoord	Uncoord	Uncoord
Body Position	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Excessive Vocalization	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Breathing Pattern	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Twitch	None	None	None	None	None	None	None	None	None	None
Tremor	None	None	None	None	None	None	None	None	None	None
Spasm	None	None	None	None	None	None	None	None	None	None
Jerks	None	None	None	None	None	None	None	None	None	None
Clonic Convulsions	None	None	None	None	None	None	None	None	None	None
Tonic Convulsions	None	None	None	None	None	None	None	None	None	None
Unusual Behavior	None	None	None	None	None	None	None	None	None	None
Arousal	Active	Hypertact	Active	InactAlert	Active	Active	Active	Active	Active	Active
Palpebral Closure	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen	WideOpen
Defecation	None	None	None	None	None	None	None	None	None	None
Urine	None	Present	None	None	None	None	None	None	None	None
Piloerection	None	None	None	None	None	None	None	None	None	None
Rears	22	26	8	0	9	10	7	10	21	8
Approach Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Startle Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Tail Pinch Response	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable	Noticable
Pupil Size	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Muscle Tone	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Lacrimation	None	None	None	None	None	None	None	None	None	None
Salivation	None	None	None	None	None	None	None	None	None	None
Fur Appearance	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal	Normal
Facial Crust	None	None	None	None	None	None	None	None	None	None
Additional Observations	None	None	None	None	None	None	None	None	None	None
Visual Placing	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
Grip Strength #1 (fore)	.21	.45	.46	.41	.40	.70	.25	.56	.49	.67
Grip Strength #2 (fore)	.22	.38	.44	.50	.41	.62	.33	.48	.54	.69
Grip Strength #1 (hind)	.27	.26	.28	.29	.34	.36	.35	.42	.42	.41
Grip Strength #2 (hind)	.25	.33	.30	.25	.33	.28	.37	.21	.45	.34
Body Temperature	38.10	39.00	38.10	37.50	38.00	38.10	37.20	37.30	38.50	38.20
Body Weight	116.30	121.68	123.12	127.60	128.92	128.90	125.18	130.36	128.96	139.32
Air Righting	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord	FeetCoord
Hind Leg Splay #1	8.00	6.60	8.30	7.40	7.20	7.00	6.20	7.40	8.00	8.50
Hind Leg Splay #2	7.40	6.00	8.60	7.30	7.10	6.80	6.60	6.30	8.70	9.00

^aSlight wobble in rear quarters when walking

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

OVERVIEW OF THE FUNCTIONAL OBSERVATIONAL BATTERY (FOB)
AND FOB SCORING CRITERIA

The FOB involved the evaluation and documentation of the absence or presence (or severity if appropriate) of a predetermined set of behavioral and clinical signs for individual animals. During examination, all animals were observed in their observation cages for signs of involuntary muscular movements (twitches, tremors, spasms, jerks, and convulsions) and evaluated for posture and palpebral closure. One animal was then removed from its observation cage and handling reactivity was evaluated. The animal was placed on an observation cart and observed for signs of ataxia, involuntary muscular movements, excessive vocalization, piloerection, and unusual behavior. Gait, body position, breathing pattern, arousal, palpebral closure, defecation, urination, and rears were also evaluated during this observation period. Approach, startle, and tail pinch responses were then evaluated while the animal was still on the observation cart. The animal was then held, and pupil size, muscle tone, lacrimation, salivation, fur appearance, crusts, and visual placing were evaluated. Any additional clinical observations were also recorded. Grip strength, body temperature, body weight, air righting reflexes, and hind leg splay were subsequently evaluated. The same evaluations were then performed for the remaining animals. The FOB required approximately 6 minutes to perform for each animal.

Two technicians evaluated and documented neurobehavioral function of the test animals while blind to the animals' treatment.

I. Cageside Observations

Abbreviations or shortened names which are used during data collection are listed in parentheses.

Posture	<p>The condition and body position of the animal in its observation cage. Scored as:</p> <ol style="list-style-type: none">1. Normal/Awake (NormAwake) - Animal was in any normal awake position; i.e., standing, sitting, or rearing.2. Normal/Asleep (NormAslee) - Animal was asleep in any normal position; i.e., lying on side or curled3. On side/Prostrate (SideProst) - Animal was on its side with its legs out to the side and appeared to be unaware of its surroundings.4. On Stomach/Prostrate (StomProst) - Animal was on its stomach with its legs splayed to the front or sides and appeared to be unaware of its surroundings.5. Other - The animal was in an abnormal or unusual position which is not included above.
----------------	--

**Palpebral
Closure**

The degree of closure of the eyelids. Scored as:

1. **Wide open (WideOpen)** - The animal's eyelids were fully open.
2. **Slightly Drooping (SlDroop)** - The animal's eyelids were slightly closed but were more than halfway open.
3. **Halfway Shut (HalfShut)** - The animal's eyelids were halfway closed or more but were not completely closed.
4. **Completely Shut (Shut)** - The animal's eyelids were completely closed.

Twitch

Brief, involuntary muscle contractions which caused the animal to abruptly move its extremities and/or individual isolated muscles or muscle groups. Recorded by location as:

1. **None**
2. **Head**
3. **Forelimbs**
4. **Hindlimbs**
5. **Other**

Further scored by severity:

1. **Present (slight; fine)**
2. **Excessive (pronounced; coarse)**

Tremor

Continual, rhythmic quivering of the skeletal muscle involving or associated with a specific area. Recorded by location as:

1. **None**
2. **Head**
3. **Forelimbs**
4. **Hindlimbs**
5. **Whole body (WholeBody)**
6. **Other**

Further scored by severity:

1. **Present (slight; fine)**
2. **Excessive (pronounced; coarse)**

Spasm

A sustained, involuntary contraction of a muscle or group of muscles without being rhythmic. Recorded by location as:

1. **None**
2. **Head**
3. **Forelimbs**
4. **Hindlimbs**
5. **Other**

Further scored by severity:

1. **Present (single occurrence of short duration)**
2. **Excessive (multiple occurrences or single occurrence of extended duration)**

Jerk

A sudden involuntary movement. Recorded by location as:

1. None
2. Head
3. Forelimbs
4. Hindlimbs
5. Whole body (WholeBody)
6. Other

Further scored by severity:

1. Present (1 or 2 occurrences)
2. Excessive (multiple occurrences)

**Clonic
Convulsions**

Involuntary, repetitive, severe contractions of the voluntary (skeletal) muscles which may have been marked by movements similar to natural purposeful movements. Recorded by the movements associated with the convulsion as:

1. None
2. Running Fits (RunFits) - The animal's limbs moved in a running movement during the convulsions.
3. Explosive Jumps (ExplJump) - The animal jumped into the air with all 4 feet leaving the surface of the cart.
4. Writhing - The animal twisted and turned.
5. Paddling - The animal's limbs moved forward and back in a swimming motion.
6. Other

Further scored by severity:

1. Present (single occurrence of short duration)
2. Excessive (multiple occurrences or single occurrence of extended duration)

**Tonic
Convulsions**

Involuntary, severe sustained contractions of the voluntary (skeletal) muscles which produced animal rigidity. Recorded as:

1. None
2. Present

Further scored by severity:

1. Present (single occurrence of short duration)
2. Excessive (multiple occurrences or single occurrence of extended duration)

II. Open Field Observations

**Handling
Reactivity**

The reaction of the animal to being removed from the observation cage and handled. Scored as:

1. Slight/Moderate Resistance (Resists) - The animal was easy to handle although it may have struggled or vocalized occasionally.
2. Animal Limp (Limp) - The animal was limp/flaccid when handled.
3. High Resistance/Aggressive (HighResis) - The animal was difficult to handle, and/or struggled continuously, and/or tried to bite.

Ataxia

The animal showed a clear loss of balance while sitting or rearing. Recorded as:

1. No
2. Yes

Further scored by severity:

1. Present - The animal repeatedly began to fall while sitting and then caught itself or the animal had some difficulty holding itself erect while rearing. The animal may have fallen occasionally.
2. Excessive - The animal fell frequently while sitting or rearing.

Gait

The animal's manner of walking. Recorded as:

1. Normal - No obvious gait impairment
2. Uncoordinated (Uncoord) - The animal's movements were uncoordinated. Further scored by severity:
 1. Present - The animal walked with a noticeable sway and/or rocking and/or jerky movements when walking. Animal may have fallen on side occasionally.
 2. Excessive - The animal frequently fell on its back and/or side while moving. The animal may not have been able to move beyond a restricted area.
3. Limbs Exaggerated/Splayed (Splayed) - The hindlimbs and/or forelimbs showed exaggerated placement or movements.

Further scored by severity:

1. Present - The animal displayed slightly abnormal placement/movement of the limbs.
2. Excessive - The limbs were moved in an extremely exaggerated motion when walking. The limbs were splayed at least 45 degrees from body.
4. Walks on Toes (OnToes) - The animal did not place its feet in a normal heel to toe manner when walking. The hindlimbs were drawn into the body. Further scored by severity:
 1. Present - There was a noticeable alteration in body position. The back may have appeared to be arched/hunched. The animal walked on its toes and the distal pads of its feet.
 2. Excessive - The animal walked only on its toes with a severely arched/hunched body position.
5. Hypotonic - The animal was unable to support its weight but was able to move in a straight line without lurching.

Further scored by severity:

1. Present - The animal moved slowly and dragged its abdomen on the surface of the observation cart.
2. Excessive - The animal's limbs were apparently weak and obviously splayed. The animal dragged its abdomen on the surface of the observation cart and had labored locomotion.
6. Other - Any other abnormality or combination of abnormalities. Further scored by severity.

Body Position

The animal's posture while in the observation cart.
Recorded as:

1. **Normal** - The animal's body position was normal.
2. **Hunched** - The animal's back was arched when standing normally or walking
3. **On side (OnSide)** - The animal lay on its side. It may have make occasional attempts to stand/walk but was unable to do so effectively.
4. **On stomach (OnStomach)** - The animal lay on its stomach with its limbs unable to support its weight. The animal may have attempted to stand/walk but was unable to so effectively.
5. **Other** - The animal was in an abnormal or unusual position which is not included above.

**Excessive
Vocalization**

The animal vocalized without being provoked or vocalized continuously while being handled. Recorded as:

1. **None**
2. **Present**

**Breathing
Pattern**

A characterization of the animal's respiration. Recorded as:

1. **Normal**
2. **Mouthbreathing (MthBreath)** - The animal appeared to have a normal breathing pattern but breathed with its mouth open.
3. **Labored** - The animal had difficulty breathing and may have appeared to be gasping.
4. **Audible** - Abnormal respiratory sounds were heard while listening to the animal breathing.
5. **Rapid respiration (Rapid)** - The animal breathed with excessively quick, short breaths.
6. **Other**

Twitch

As described above.

Tremor

As described above.

Spasm

As described above.

Jerk

As described above.

**Clonic
Convulsions**

As described above.

**Tonic
Convulsions**

As described above.

**Unusual
Behavior**

Behavior which occurred out of context and/or with abnormally high frequency or behaviors not associated with the normal repertoire of the species. Recorded as:

1. None
2. Retropulsion (Retropuls) - The animal walked backward.
3. Head Bobbing/Weaving (HeadBob) - The animal moved its head up and down or from side to side continuously.
4. Stereotypy (Stereotyp) - The animal performed a normal behavior for an unusually long time.
5. Prostrate - The animal was lying down and showed little or no spontaneous movement. The animal appeared to be unaware of its surroundings, but was apparently awake.
6. Other

Arousal

An assessment of the level of unprovoked activity and alertness in the observation cart. Recorded as:

1. Active/alert (Active) - The animal went through a normal repertoire of behaviors consisting of periods of sniffing, rearing, exploring, grooming, etc.
2. Hyperactive/hyperalert (Hyperact) - The animal appeared excited and may have darted or froze during the observation period or may have sat in one place and jumped at any sound or movement.
3. Inactive/alert (InacAlert) - The animal generally sat in one place during the majority of the observation period but appeared to be aware of its surroundings.
4. Inactive/not alert (NotAlert) - The animal sat in one place during the observation period and appeared to be unaware of its surroundings or was in a stupor.

**Palpebral
Closure**

As described above.

Defecation

The type or absence of excrement during the observation. Recorded as:

1. None
2. Normal
3. Soft
4. Diarrhea

Urine

The amount of urination during the observation period.

1. None
2. Present
3. Excessive

Piloerection

The animal's hair stood vertical to the plane of the skin surface. Recorded as:

1. None
2. Present

Rears

The number of times the animal lifted both front legs off the surface of the cart during the observation period. Any time the animal placed one or both front paws on the surface of the cart and then removes it/them another rear was counted.

III. Manipulative Observations**Approach
Response**

The animal's reaction to being approached by an object. The animal was approached at nose level with the end of a blunt object. The object was stopped approximately 3-4 cm from the animal's nose and held there for several seconds without making contact with the animal. The animal's reaction was recorded as:

1. **Noticeable reaction (Noticable)** - The animal froze, slowly approached the object, sniffed the object, or turned away from the object.
2. **No reaction (None)** - The animal made no noticeable reaction and apparently did not care or recognize that the object was there.
3. **Exaggerated reaction (Exagger)** - The animal attacked or fled from the object

**Startle
Response**

The animal's response to acoustic stimuli. A hand held metal clicker was positioned approximately 5 cm above the animal and held out of sight. The clicker was quickly clicked and the animal's reaction was recorded as:

1. **Noticeable reaction (Noticable)** - The animal made a noticeable reaction. This reaction may have ranged from a slight flick of the ears to an obvious flinch.
2. **No reaction (None)** - The animal made no noticeable reaction.
3. **Exaggerated reaction (Exagger)** - The animal jumped at the sound or fled from the sound. Generally, the animal's front feet left the surface of the cart for a jump to have been considered an exaggerated reaction.

**Tail Pinch
Response**

A pair of tweezers was used to pinch the tail approximately 2-3 cm from the tip. The animal's reaction to having its tail pinched was recorded as:

1. **Noticeable reaction (Noticable)** - The animal made a noticeable reaction. The animal may have flinched, walked away, or turned toward its tail.
2. **No reaction (None)** - The animal made no noticeable reaction.
3. **Exaggerated reaction (Exagger)** - The animal jumped, fled, or turned and attacked the tweezers or the technician's hand.

Pupil Size

The pupil's relative size to the normal size for the test species. The animal's eye was held open and the size of the pupil was recorded as:

1. **Normal** - The pupil was less than approximately 50% of the eyeball but was not pinpoint.
2. **Increased** - The pupil was at least 50% of the eyeball.
3. **Decreased** - The pupil was pinpoint.

Muscle Tone

The animal was held and the technician felt the abdominal musculature and moved the hind legs to determine the range of their movement and resiliency. The relative rigidity or flaccidity of the limb and abdominal musculature was recorded as:

1. **Normal** - The animal's muscles were resilient and firm and the hindlimbs went through their full range of movement.
2. **Increased** - The animal's muscles were rigid and the hindlimbs would not go through their full range of movements.
3. **Decreased** - The animal's muscles were flaccid and the hindlimbs had no resistance to movement.

Lacrimation

Secretion or discharge of tears causing the fur to appear wet around the eyes. Recorded as:

1. **None**
2. **Present** - Lacrimation was noticeable.
3. **Excessive** - The animal had a large amount of tearing.

Salivation

The presence of saliva around the mouth.

1. **None**
2. **Present** - Salivation was noticeable around the edges of the mouth.
3. **Excessive** - The salivation extended to the fur around the jaw.

Fur Appearance

The appearance of the animal's fur.

1. **Normal**
2. **Unkempt** - The animal had an unusually rough or ungroomed appearance.
3. **Urine Stains/Wetness (UrinStain)** - The animal's fur had stains or was wet from the discharge of urine.
4. **Other** - Any other discoloration or abnormal condition of the animal's fur.

Facial Crust

The presence or absence of a crust around the mouth, nose, or eyes. Recorded by location as:

1. **None**
2. **Eyes**
3. **Nose**
4. **Mouth**
5. **Multiple areas (Multiple)** - More than one location had a crust present.

**Additional
Observations**

Any additional clinical observations were recorded as:

1. None
2. ~~Emaciation~~ (Emaciated) - An excessively lean appearance.
3. Dehydration (Dehydrat) - An abnormal depletion of body fluid. When present, if the animal's skin was pinched it remains in a pinched position when released.
4. Exophthalmus (Exophthal) - An abnormal protrusion of the eyeball from the eye socket.
5. Other - Additional observations, not included above, were present or more than 1 of the above observations were present.

Visual Placing

The presence or absence of forelimb extension in anticipation of grasping a surface while being held by the observer. The observer's palm was on the back of the animal with the fingers wrapped around the animal's midsection. The animal was held level with forelimb grip strength strain gauge (described below) with its body parallel to the floor. The animal was then slowly moved toward the strain gauge and the presence or absence of forelimb extension was recorded as:

1. Present
2. None

Grip Strength

The force, in kg, necessary to break the animal's grip on a wire screen attached to a strain gauge. Two strain gauges with wire mesh screens were secured to a Plexiglas® stand. One gauge was positioned parallel to the floor (forelimb gauge) and other was angled slightly down toward the floor (hindlimb gauge). The limbs to be tested were placed on the screen and the animal was allowed to grasp the screen with its toes. The animal was then pulled smoothly until its grip was broken and the reading of the strain gauge was recorded. Two trials were performed for the forelimbs and the hindlimbs.

Body Temperature

Core body temperature was measured using a digital thermometer. A vinyl rectal probe was dipped into petroleum jelly and inserted through the animal's rectum (approximately 6-8 cm depending on the size of the rat). The temperature in °C was recorded when the gauge had stabilized. The probe was wiped clean between animals.

Body Weight

The animal's body weight, in grams, was recorded using an electronic balance.

Air Righting

The ability of the animal to right itself while airborne. The animal was held upside down parallel to the surface of a padded cart with the observer's hands under its back. The animal was held approximately 30 cm above the surface of the cart and released. The test was not performed if the animal was considered by the observer to be impaired to the point that it could be injured if dropped. The manner in which the animal landed was recorded as:

1. **Feet/Coordinated (FeetCoord)** - The animal landed on its feet and appeared to have no problem with balance
2. **Feet/Uncoordinated (FeetUncoor)** - The animal landed on its feet but stumbled or staggered after landing.
3. **Side** - The animal landed on its side.
4. **Back** - The animal landed on its back.

Hind Leg Splay

The outside digit pads of the animal's hind paws were painted using non-toxic paint. The animal was then held in a prone position (the fingers of one hand under the animal's forelimbs and the other hand holding the base of its tail) approximately 40 cm above a cart. The animal was dropped 2 times onto a piece of paper and the paint marks left by the animals digit pads were marked. The distance, in cm, between the 2 paint marks (measured from the center of each paint mark) for each landing was recorded

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

FOB STATISTICAL SUMMARY

I. BMDP P7D:

The data for parameters that generate continuous data were intercompared for the dose and control groups by use of Levene's test for homogeneity of variances, by analysis of variance, and by pooled variance t-tests. The t-tests were used, if the analysis of variance was significant, to delineate which groups differed from the control groups. If Levene's test indicated heterogeneous variances, the groups were compared by an analysis of variance for unequal variances followed, if necessary, by separate variance t-tests.

II. BMDP P4F:

The incidence data were analyzed for group effects using Fisher's Exact Test on 2x2 tables.

Incidence data were collapsed to a single category, if necessary, prior to 2x2 table analysis (absence versus presence of a finding or normal versus abnormal). More than one response for a selected parameter may be considered normal and some parameters can be evaluated as either normal versus abnormal or present versus absent. The way in which the parameters were evaluated was determined after reviewing the data tables.

Additional analyses were performed on selected incidence data with ordered severity scores which do not conform to collapse into a 2x2 table analysis. For these, Gamma, Kendall's Tau-B, Stuart's Tau-C, and Somers' D measures of association were computed.

Summary of the category designation for certain frequency parameters and additional P4F analyses in this study:

Cage Posture - Evaluated with awake as normal and asleep or any other finding as abnormal.

Cage Palpebral Closure - Any response could be considered normal; therefore, a P4F analysis examining the correlation between amount of closure and dose level was performed.

Handling Reactivity - Slight/moderate resistance was considered normal; any other response was considered abnormal.

Arousal - Alternating behaviors was considered normal; any other response was considered abnormal.

Urine - Evaluated as absent versus present.

Approach, Startle, and Tail Pinch Responses - Noticeable reactions were considered normal; any other response was considered abnormal.

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

Individual Anatomic Pathology Data

(49 Pages)

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TABLE 1
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

NECROPSY PROTOCOL

NONPERFUSED MALES

The following tissues were examined at necropsy with no significant lesions observed unless specified on individual animal page:

TOTAL BODY	ADIPOSE TISSUE	MESENTERY/OM'TUM	PERITONEUM	PERITONEAL CAV
PLEURA	THORACIC CAV	HEART	PERICARDIAL CAV	AORTA
VASCULATURE	SALIVARY GL	TONGUE	ESOPHAGUS	STOMACH
LIVER	PANCREAS	DUODENUM	JEJUNUM	ILEUM
CECUM	COLON*	RECTUM	ANUS	PITUITARY
THYROID GL	PARATHYROID GL	ADRENAL GL	SKIN	SUBCUTIS
HEAD	EARS	NARES/NQSE	MAMMARY GL	PAWS/FEET
TAIL	SPLEEN	LYMPH ND, S-MAN	LYMPH ND, MED	LYMPH ND, MES
THYMIC REGION	BONE/JOINT	BONE, STERNUM	BONE, FEMUR	BONE, VERTEBRA
BONE MARROW	SKELETAL MUSCLE	DIAPHRAGM	BRAIN	SPINAL CORD
NERVE, SCIATIC	EYE	HARDERIAN GL	LACRIMAL GL	TESTES
EPIDIDYMIDES	VASA DEFERENTIA	SEMINAL VESICLE	PROSTATE	PENIS
LARYNX	TRACHEA	LUNGS	KIDNEYS	URETER
URINARY BLADDER	URETHRA	GROSS LESIONS		

The following organs were weighed at necropsy:

HEART	LIVER	ADRENAL GL	SPLEEN	BRAIN
TESTES	LUNGS	KIDNEYS		

The microscopic procedures used in this study are described in the methods section of the text.

Micro diagnosis grade codes:

1=MINIMAL, 2=MILD, 3=MODERATE, 4=MARKED, 5=SEVERE, P=PRESENT

Micro diagnosis distribution codes:

()=FOCAL, (())=MULTIFOCA, NO PARENTHESES=DIFFUSE

Micro diagnosis prefix codes:

= NEOPLASM, B = BENIGN, M = MALIGNANT, @PN = PRE-NEOPLASTIC

MICRO+ indicates histologic confirmation of preceding gross diagnosis.

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

NONPERFUSED			
GROUP:	0 PPM	MALE	
<u>ANIMAL</u>	<u>717</u>	<u>10-MAR-94</u>	<u>STUDY DAY 11</u>
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE			
GROSS: NOT EXAMINED			
MICRO: NOT EXAMINED			
<u>ANIMAL</u>	<u>735</u>	<u>12-MAR-94</u>	<u>STUDY DAY 13</u>
TYPE OF DEATH: SCHEDULED SACRIFICE			
<u>ORGAN WEIGHT</u>	<u>ABS.(G)</u>	<u>REL.</u>	<u>BRAIN</u>
LIVER	7.845	4.362	GROSS: MENINGEAL HEMORRHAGE
KIDNEYS	1.432	0.796	SLIGHT
LUNGS	0.936	0.520	MICRO: ((1)) VACUOLATION/SPONGIOSIS
SPLEEN	0.417	0.232	CEREBELLAR WHITE MATTER NEAR
HEART	0.649	0.361	VESTIBULAR NUCLEI
BRAIN	1.797	0.999	UNILATERAL
ADRENAL GL	0.044	0.024	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
TESTES	1.998	1.111	HEART ORAL/PHARYNGEAL STOMACH
TERMINAL BODY WT.	179.8		LIVER ADRENAL GL SPLEEN
			SPINAL CORD NERVE, SCIATIC TESTES
			NASAL CAVITY LARYNX TRACHEA
			LUNGS KIDNEYS URINARY BLADDER
<u>ANIMAL</u>	<u>752</u>	<u>12-MAR-94</u>	<u>STUDY DAY 13</u>
TYPE OF DEATH: SCHEDULED SACRIFICE			
<u>ORGAN WEIGHT</u>	<u>ABS.(G)</u>	<u>REL.</u>	<u>SKIN</u>
LIVER	8.035	4.390	GROSS: CRUST/SCAB/SCALE
KIDNEYS	1.426	0.779	RED CRUST, PERINASAL AREA
LUNGS	0.923	0.504	BRAIN
SPLEEN	0.492	0.269	GROSS: MENINGEAL HEMORRHAGE
HEART	0.630	0.344	MODERATE
BRAIN	1.707	0.933	URINARY BLADDER
ADRENAL GL	0.040	0.022	MICRO: P INTRALUMINAL PROTEIN COAGULUM
TESTES	2.251	1.230	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
TERMINAL BODY WT.	183.0		HEART ORAL/PHARYNGEAL STOMACH
			LIVER ADRENAL GL SKIN
			SPLEEN BRAIN SPINAL CORD
			NERVE, SCIATIC TESTES NASAL CAVITY
			LARYNX TRACHEA LUNGS
			KIDNEYS
<u>ANIMAL</u>	<u>715</u>	<u>10-MAR-94</u>	<u>STUDY DAY 11</u>
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE			
GROSS: NOT EXAMINED			
MICRO: NOT EXAMINED			
<u>ANIMAL</u>	<u>711</u>	<u>12-MAR-94</u>	<u>STUDY DAY 13</u>
TYPE OF DEATH: SCHEDULED SACRIFICE			
<u>ORGAN WEIGHT</u>	<u>ABS.(G)</u>	<u>REL.</u>	<u>GROSS: EXAMINED - NO SIGNIFICANT LESIONS</u>
LIVER	8.504	4.292	LUNGS
KIDNEYS	1.562	0.788	MICRO: ((1)) ALVEOLAR HISTIOCYTOSIS
LUNGS	0.849	0.428	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
SPLEEN	0.482	0.243	HEART ORAL/PHARYNGEAL STOMACH
HEART	0.683	0.345	LIVER ADRENAL GL SPLEEN
BRAIN	1.792	0.904	BRAIN SPINAL CORD NERVE, SCIATIC

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 PPM MALE			NONPERFUSED		
<hr/>					
<u>ANIMAL 711 (CONTINUED)</u>					
ADRENAL GL	0.039	0.020	TESTES	NASAL CAVITY	LARYNX
TESTES	2.551	1.287	TRACHEA	KIDNEYS	URINARY BLADDER
TERMINAL BODY WT.	198.1				
<hr/>					
<u>ANIMAL 750 10-MAR-94</u>			<u>STUDY DAY 11</u>		
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE					
			GROSS: NOT EXAMINED		
			MICRO: NOT EXAMINED		
<hr/>					
<u>ANIMAL 751 10-MAR-94</u>			<u>STUDY DAY 11</u>		
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE					
			GROSS: NOT EXAMINED		
			MICRO: NOT EXAMINED		
<hr/>					
<u>ANIMAL 706 12-MAR-94</u>			<u>STUDY DAY 13</u>		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	SKIN		
LIVER	9.484	4.780	GROSS: CRUST/SCAB/SCALE		
KIDNEYS	1.707	0.860	BROWN CRUST ON THE LEFT PERINASAL		
LUNGS	1.050	0.529	REGION 3X4X3 MM		
SPLEEN	0.496	0.250	SKELETAL MUSCLE		
HEART	0.680	0.343	GROSS: TRAUMATIZED		
BRAIN	1.725	0.869	TISSUE AROUND THE LEFT EYE SOCKET,		
ADRENAL GL	0.045	0.023	DUE TO BLEEDING		
TESTES	2.508	1.264	BRAIN		
TERMINAL BODY WT.	198.4		MICRO: ((1)) VACUOLATION/SPONGIOSIS		
			UNILATERAL FOCUS, CEREBELLAR NUCLEI		
			LUNGS		
			MICRO: ((2)) ALVEOLAR HISTIOCYTOSIS		
			URINARY BLADDER		
			MICRO: (P) INTRALUMINAL PROTEIN COAGULUM		
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
			HEART	ORAL/PHARYNGEAL	STOMACH
			LIVER	ADRENAL GL	SKIN
			SPLEEN	SPINAL CORD	NERVE, SCIATIC
			TESTES	NASAL CAVITY	LARYNX
			TRACHEA	KIDNEYS	
			THE FOLLOWING TISSUES WERE MISSING:		
			SKELETAL MUSCLE		
<hr/>					
<u>ANIMAL 738 10-MAR-94</u>			<u>STUDY DAY 11</u>		
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE					
			GROSS: NOT EXAMINED		
			MICRO: NOT EXAMINED		
<hr/>					
<u>ANIMAL 728 12-MAR-94</u>			<u>STUDY DAY 13</u>		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	GROSS: EXAMINED - NO SIGNIFICANT LESIONS		
LIVER	9.780	4.482	SPINAL CORD		
KIDNEYS	1.795	0.823	MICRO: MICROSCOPICALLY NORMAL		

See necropsy protocol page for list of tissues examined grossly and for explanation of grade

See necropsy protocol page for list of tissues examined grossly and for explanation of grades

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 PPM MALE			NONPERFUSED		

ANIMAL	728 (CONTINUED)				
LUNGS	1.066	0.489	LONGITUDINAL SECTION HAS CONSIDERABLE		
SPLEEN	0.511	0.234	ARTIFACT		
HEART	0.796	0.365	LUNGS		
BRAIN	1.847	0.847	MICRO: ((1)) ALVEOLAR HISTIOCYTOSIS		
ADRENAL GL	0.044	0.020	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
TESTES	2.646	1.213	HEART	ORAL/PHARYNGEAL	STOMACH
TERMINAL BODY WT.	218.2		LIVER	ADRENAL GL	SPLEEN
			BRAIN	SPINAL CORD	NERVE, SCIATIC
			TESTES	NASAL CAVITY	LARYNX
			TRACHEA	KIDNEYS	URINARY BLADDER

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 100 PPM		MALE		NONPERFUSED	

ANIMAL	740	12-MAR-94	STUDY DAY 13		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	BRAIN		
LIVER	7.975	4.454	GROSS: MENINGEAL HEMORRHAGE		
KIDNEYS	1.472	0.822	MODERATE		
LUNGS	0.896	0.500	MICRO: EXAMINED - NO SIGNIFICANT LESIONS		
SPLEEN	0.474	0.265	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
HEART	0.685	0.383	BRAIN SPINAL CORD		
BRAIN	1.771	0.989			
ADRENAL GL	0.039	0.022			
TESTES	1.683	0.940			
TERMINAL BODY WT.	179.1				
ANIMAL	714	12-MAR-94	STUDY DAY 13		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	BRAIN		
LIVER	7.835	4.393	GROSS: MENINGEAL HEMORRHAGE		
KIDNEYS	1.486	0.833	MILD		
LUNGS	0.827	0.464	MICRO: EXAMINED - NO SIGNIFICANT LESIONS		
SPLEEN	0.445	0.249	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
HEART	0.593	0.332	BRAIN SPINAL CORD		
BRAIN	1.726	0.968			
ADRENAL GL	0.041	0.023			
TESTES	2.162	1.212			
TERMINAL BODY WT.	178.4				
ANIMAL	745	10-MAR-94	STUDY DAY 11		
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE					
GROSS: NOT EXAMINED					
MICRO: NOT EXAMINED					
ANIMAL	703	10-MAR-94	STUDY DAY 11		
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE					
GROSS: NOT EXAMINED					
MICRO: NOT EXAMINED					
ANIMAL	725	12-MAR-94	STUDY DAY 13		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	SKIN		
LIVER	7.805	4.403	GROSS: CRUST/SCAB/SCALE		
KIDNEYS	1.498	0.845	RED, PERINASAL REGION		
LUNGS	0.877	0.495	LYMPH ND, S-MAN		
SPLEEN	0.459	0.259	GROSS: COLOR CHANGE, DIFFUSE		
HEART	0.646	0.364	ALL NODES, RED		
BRAIN	1.738	0.980	MICRO: EXAMINED - NO SIGNIFICANT LESIONS		
ADRENAL GL	0.036	0.020	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
TESTES	2.106	1.188	BRAIN SPINAL CORD		
TERMINAL BODY WT.	177.3				

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 100 PPM MALE NONPERFUSED

ANIMAL 709 10-MAR-94 STUDY DAY 11

TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE

GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

ANIMAL 755 10-MAR-94 STUDY DAY 11

TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE

GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

ANIMAL 716 12-MAR-94 STUDY DAY 13

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	8.812	4.453
KIDNEYS	1.568	0.792
LUNGS	0.883	0.446
SPLEEN	0.477	0.241
HEART	0.633	0.320
BRAIN	1.808	0.914
ADRENAL GL	0.039	0.020
TESTES	2.452	1.239
TERMINAL BODY WT.	197.9	

SKIN
GROSS: CRUST/SCAB/SCALE
RED CRUST, RIGHT PERIOcular AREA
BRAIN
MICRO: ((2)) MENINGEAL HEMORRHAGE
((1)) BRAIN HEMORRHAGE
LUNGS
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
2X2 MM DARK RED FOCUS, RIGHT CARDIAC
LOBE

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
SPINAL CORD

ANIMAL 736 12-MAR-94 STUDY DAY 13

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	8.783	4.413
KIDNEYS	1.626	0.817
LUNGS	1.007	0.506
SPLEEN	0.507	0.255
HEART	0.758	0.381
BRAIN	1.758	0.883
ADRENAL GL	0.059	0.030
TESTES	2.577	1.295
TERMINAL BODY WT.	199.0	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
BRAIN
SPINAL CORD

ANIMAL 719 10-MAR-94 STUDY DAY 11

TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE

GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 500 PPM MALE

NONPERFUSED

ANIMAL 743 10-MAR-94 STUDY DAY 11

TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE

GROSS: NOT EXAMINED

MICRO: NOT EXAMINED

ANIMAL 757 12-MAR-94 STUDY DAY 13

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT ABS.(G) REL.

LIVER 9.593 4.973

KIDNEYS 1.629 0.844

LUNGS 0.953 0.494

SPLEEN 0.531 0.275

HEART 0.737 0.382

BRAIN 1.723 0.893

ADRENAL GL 0.040 0.021

TESTES 2.496 1.294

TERMINAL BODY WT. 192.9

GROSS: EXAMINED - NO SIGNIFICANT LESIONS

MICRO: EXAMINED - NO SIGNIFICANT LESIONS

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

BRAIN SPINAL CORD

ANIMAL 720 12-MAR-94 STUDY DAY 13

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT ABS.(G) REL.

LIVER 7.129 4.382

KIDNEYS 1.407 0.865

LUNGS 0.842 0.518

SPLEEN 0.416 0.256

HEART 0.674 0.414

BRAIN 1.731 1.064

ADRENAL GL 0.039 0.024

TESTES 2.107 1.295

TERMINAL BODY WT. 162.7

SKIN

GROSS: CRUST/SCAB/SCALE

RED, AROUND LEFT EYE

LYMPH ND, S-MAN

GROSS: COLOR CHANGE, DIFFUSE

SEVERAL NODES, RED

EYE

GROSS: TRAUMATIZED

LEFT, DUE TO BLEEDING

MICRO: EXAMINED - NO SIGNIFICANT LESIONS

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

BRAIN SPINAL CORD

ANIMAL 710 10-MAR-94 STUDY DAY 11

TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE

GROSS: NOT EXAMINED

MICRO: NOT EXAMINED

ANIMAL 731 10-MAR-94 STUDY DAY 11

TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE

GROSS: NOT EXAMINED

MICRO: NOT EXAMINED

ANIMAL 730 12-MAR-94 STUDY DAY 13

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT ABS.(G) REL.

LIVER 8.785 4.600

KIDNEYS 1.625 0.851

LUNGS 0.943 0.494

SPLEEN 0.502 0.263

HEART 0.696 0.364

SKIN

GROSS: CRUST/SCAB/SCALE

RED CRUST, PERINASAL AND PERIOULAR

REGIONS (BILATERAL)

LYMPH ND, S-MAN

GROSS: COLOR CHANGE, DIFFUSE

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 500 PPM			MALE		NONPERFUSED	
<hr/>						
ANIMAL		730 (CONTINUED)				
BRAIN	1.801	0.943	SEVERAL NODES, RED			
ADRENAL GL	0.053	0.028	BRAIN			
TESTES	2.417	1.266	MICRO: (2)	BRAIN HEMORRHAGE		
TERMINAL BODY WT.	191.0		EYE			
			GROSS:	TRAUMATIZED		
			LEFT, DUE TO BLEEDING			
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
			SPINAL CORD			
<hr/>						
ANIMAL		722	10-MAR-94	STUDY DAY	11	
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE						
GROSS: NOT EXAMINED						
MICRO: NOT EXAMINED						
<hr/>						
ANIMAL		721	10-MAR-94	STUDY DAY	11	
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE						
GROSS: NOT EXAMINED						
MICRO: NOT EXAMINED						
<hr/>						
ANIMAL		713	12-MAR-94	STUDY DAY	13	
TYPE OF DEATH: SCHEDULED SACRIFICE						
ORGAN WEIGHT	ABS.(G)	REL.				
LIVER	9.435	4.772	GROSS:	EXAMINED - NO SIGNIFICANT LESIONS		
KIDNEYS	1.639	0.829	MICRO:	EXAMINED - NO SIGNIFICANT LESIONS		
LUNGS	0.852	0.431	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
SPLEEN	0.477	0.241	BRAIN			
HEART	0.658	0.333	SPINAL CORD			
BRAIN	1.663	0.841				
ADRENAL GL	0.034	0.017				
TESTES	2.588	1.309				
TERMINAL BODY WT.	197.7					
<hr/>						
ANIMAL		724	12-MAR-94	STUDY DAY	13	
TYPE OF DEATH: SCHEDULED SACRIFICE						
ORGAN WEIGHT	ABS.(G)	REL.	SKIN			
LIVER	9.656	4.812	GROSS:	CRUST/SCAB/SCALE		
KIDNEYS	1.725	0.860	RED CRUST, PERINASAL AND LEFT			
LUNGS	0.959	0.478	PERIOULAR REGION			
SPLEEN	0.479	0.239	MICRO:	EXAMINED - NO SIGNIFICANT LESIONS		
HEART	0.697	0.347	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
BRAIN	1.724	0.859	BRAIN			
ADRENAL GL	0.036	0.018	SPINAL CORD			
TESTES	2.628	1.310				
TERMINAL BODY WT.	200.7					

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 PPM MALE			NONPERFUSED	
<u>ANIMAL</u>	<u>733</u>	<u>12-MAR-94</u>	<u>STUDY DAY</u>	<u>13</u>
TYPE OF DEATH: SCHEDULED SACRIFICE				
<u>ORGAN WEIGHT</u>	<u>ABS.(G)</u>	<u>REL.</u>	<u>SKIN</u>	
LIVER	9.145	5.708	GROSS: CRUST/SCAB/SCALE	
KIDNEYS	1.454	0.908	RED CRUST, PERIOCLAR AREA, BILATERAL	
LUNGS	0.868	0.542	<u>BRAIN</u>	
SPLEEN	0.419	0.262	MICRO: ((2)) VACUOLATION/SPONGIOSIS	
HEART	0.631	0.394	MAINLY BRAINSTEM	
BRAIN	1.662	1.037	<u>SPINAL CORD</u>	
ADRENAL GL	0.030	0.019	MICRO: ((3)) VACUOLATION/SPONGIOSIS	
TESTES	1.869	1.167	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
TERMINAL BODY WT.	160.2		HEART	ORAL/PHARYNGEAL STOMACH
			LIVER	ADRENAL GL SKIN
			SPLEEN	NERVE, SCIATIC TESTES
			NASAL CAVITY	LARYNX TRACHEA
			LUNGS	KIDNEYS URINARY BLADDER
<u>ANIMAL</u>	<u>729</u>	<u>10-MAR-94</u>	<u>STUDY DAY</u>	<u>11</u>
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE				
GROSS: NOT EXAMINED				
MICRO: NOT EXAMINED				
<u>ANIMAL</u>	<u>712</u>	<u>10-MAR-94</u>	<u>STUDY DAY</u>	<u>11</u>
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE				
GROSS: NOT EXAMINED				
MICRO: NOT EXAMINED				
<u>ANIMAL</u>	<u>727</u>	<u>10-MAR-94</u>	<u>STUDY DAY</u>	<u>11</u>
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE				
GROSS: NOT EXAMINED				
MICRO: NOT EXAMINED				
<u>ANIMAL</u>	<u>739</u>	<u>10-MAR-94</u>	<u>STUDY DAY</u>	<u>11</u>
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE				
GROSS: NOT EXAMINED				
MICRO: NOT EXAMINED				
<u>ANIMAL</u>	<u>744</u>	<u>12-MAR-94</u>	<u>STUDY DAY</u>	<u>13</u>
TYPE OF DEATH: SCHEDULED SACRIFICE				
<u>ORGAN WEIGHT</u>	<u>ABS.(G)</u>	<u>REL.</u>	GROSS: EXAMINED - NO SIGNIFICANT LESIONS	
LIVER	11.116	5.826	<u>BRAIN</u>	
KIDNEYS	1.791	0.939	MICRO: ((2)) VACUOLATION/SPONGIOSIS	
LUNGS	1.094	0.573	MEDIAL LONGITUDINAL FASCICULUS OF	
SPLEEN	0.499	0.262	MEDULLA AND A FEW	
HEART	0.748	0.392	SITES OF MEDIAL MIDBRAIN.	
BRAIN	1.761	0.923	THE PONS SECTION IS MISSING	
ADRENAL GL	0.057	0.030	ALSO PRESENT IN TRIGEMINAL TRACTS	
TESTES	2.276	1.193	<u>SPINAL CORD</u>	
TERMINAL BODY WT.	190.8		MICRO: ((4)) VACUOLATION/SPONGIOSIS	
			VENTRAL/LATERAL FUNICULI	
			TRACHEA	

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 PPM MALE NONPERFUSED

ANIMAL 744 (CONTINUED)

MICRO: (2) TRACHEITIS
LUNGS
MICRO: ((1)) ALVEOLAR HISTIOCYTOSIS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
HEART ORAL/PHARYNGEAL STOMACH
LIVER ADRENAL GL SPLEEN
NERVE, SCIATIC TESTES NASAL CAVITY
LARYNX KIDNEYS URINARY BLADDER

ANIMAL 737 12-MAR-94 STUDY DAY 13

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	9.067	5.215
KIDNEYS	1.616	0.929
LUNGS	0.883	0.508
SPLEEN	0.389	0.224
HEART	0.683	0.393
BRAIN	1.729	0.994
ADRENAL GL	0.046	0.026
TESTES	2.399	1.380
TERMINAL BODY WT.	173.9	

SKIN
GROSS: SWOLLEN
MILD, BILATERAL, PERIOULAR TISSUE
MICRO+ 3 SUBCUTANEOUS EDEMA
1 SKIN SECTION AFFECTED
SKIN
GROSS: CRUST/SCAB/SCALE
RED, RIGHT PERIOULAR TISSUE, MILD
MICRO+((3)) BLEPHARITIS
THIS LESION IS DUE TO THE INFECTED EYE
BRAIN
MICRO: ((3)) VACUOLATION/SPONGIOSIS
MAINLY BRAIN STEM AT ALL LEVELS,
SLIGHT IN TRIGEMINAL
TRACTS AND MIDBRAIN
SPINAL CORD
MICRO: ((3)) VACUOLATION/SPONGIOSIS
EXTENSIVE AND FAIRLY DIFFUSE IN THE
VENTRAL/LATERAL FUNICULI
((3)) AXON DEGENERATION/FRAGMENTATION
EYE
GROSS: TRAUMATIZED
RIGHT, DUE TO BLEEDING
MICRO+ (4) CORNEAL ULCER
MICRO: (3) HYPHEMA/HEMORRHAGE
(4) KERATITIS
1 EYE IS BOTH TRAUMATIZED AND INFECTED
(4) HYPOPYON
4 CONJUNCTIVITIS
NASAL CAVITY
MICRO: (2) DACRYSOLENTITIS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
HEART ORAL/PHARYNGEAL STOMACH
LIVER ADRENAL GL SPLEEN
NERVE, SCIATIC TESTES LARYNX
TRACHEA LUNGS KIDNEYS
URINARY BLADDER

ANIMAL 723 12-MAR-94 STUDY DAY 13

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	11.296	5.913
KIDNEYS	1.710	0.895

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
BRAIN
MICRO: ((2)) VACUOLATION/SPONGIOSIS

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 PPM MALE			NONPERFUSED		
ANIMAL	723 (CONTINUED)				
LUNGS	1.007	0.527			VESTIBULAR NUCLEI, BRAINSTEM,
SPLEEN	0.427	0.224			POSSIBLE SLIGHT OPTIC
HEART	0.726	0.380			CHIASM
BRAIN	1.716	0.898	SPINAL CORD		
ADRENAL GL	0.051	0.027	MICRO: ((3))	VACUOLATION/SPONGIOSIS	
TESTES	2.295	1.201	LUNGS		
TERMINAL BODY WT.	191.0		MICRO: ((1))	ALVEOLAR HISTIOCYTOSIS	
			2	LYMPHOID HYPERPLASIA	
			URINARY BLADDER		
			MICRO: 3	ECTASIA	
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
			HEART	ORAL/PHARYNGEAL	STOMACH
			LIVER	ADRENAL GL	SPLEEN
			NERVE, SCIATIC	TESTES	NASAL CAVITY
			LARYNX	TRACHEA	KIDNEYS
ANIMAL	732	10-MAR-94	STUDY DAY	11	
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE					
			GROSS:	NOT	EXAMINED
			MICRO:	NOT	EXAMINED
ANIMAL	746	12-MAR-94	STUDY DAY	13	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	SKIN		
LIVER	11.029	5.694	GROSS:	CRUST/SCAB/SCALE	
KIDNEYS	1.757	0.907		RED CRUST, RIGHT PERIOcular AREA	
LUNGS	0.961	0.496	BRAIN		
SPLEEN	0.499	0.258	MICRO: ((2))	VACUOLATION/SPONGIOSIS	
HEART	0.814	0.420		TRIGEMINAL TRACTS AND BRAINSTEM	
BRAIN	1.664	0.859	SPINAL CORD		
ADRENAL GL	0.039	0.020	MICRO: ((4))	VACUOLATION/SPONGIOSIS	
TESTES	2.208	1.140	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
TERMINAL BODY WT.	193.7		HEART	ORAL/PHARYNGEAL	STOMACH
			LIVER	ADRENAL GL	SKIN
			SPLEEN	NERVE, SCIATIC	TESTES
			NASAL CAVITY	LARYNX	TRACHEA
			LUNGS	KIDNEYS	URINARY BLADDER

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

NECROPSY PROTOCOL
NONPERFUSED FEMALES

The following tissues were examined at necropsy with no significant lesions observed unless specified on individual animal page:

TOTAL BODY	ADIPOSE TISSUE	MESENTERY/OM'TUM	PERITONEUM	PERITONEAL CAV
PLEURA	THORACIC CAV	HEART	PERICARDIAL CAV	AORTA
VASCULATURE	SALIVARY GL	TONGUE	ESOPHAGUS	STOMACH
LIVER	PANCREAS	DUODENUM	JEJUNUM	ILEUM
CECUM	COLON	RECTUM	ANUS	PITUITARY
THYROID GL	PARATHYROID GL	ADRENAL GL	SKIN	SUBCUTIS
HEAD	EARS	NARES/NOSE	MAMMARY GL	PAWS/FEET
TAIL	SPLEEN	LYMPH ND, S-MAN	LYMPH ND, MED	LYMPH ND, MES
THYMIC REGION	BONE/JOINT	BONE, STERNUM	BONE, FEMUR	BONE, VERTEBRA
BONE MARROW	SKELETAL MUSCLE	DIAPHRAGM	BRAIN	SPINAL CORD
NERVE, SCIATIC	EYE	HARDERIAN GL	LACRIMAL GL	OVARIES
OVIDUCT	UTERUS	CERVIX	VAGINA	VULVA
LARYNX	TRACHEA	LUNGS	KIDNEYS	URETER
URINARY BLADDER	URETHRA	GROSS LESIONS		

The following organs were weighed at necropsy:

HEART	LIVER	ADRENAL GL	SPLEEN	BRAIN
OVARIES	LUNGS	KIDNEYS		

The microscopic procedures used in this study are described in the methods section of the text.

Micro diagnosis grade codes:

1=MINIMAL, 2=MILD, 3=MODERATE, 4=MARKED, 5=SEVERE, P=PRESENT

Micro diagnosis distribution codes:

()=FOCAL, (())=MULTIFOCA, NO PARENTHESES=DIFFUSE

Micro diagnosis prefix codes:

= NEOPLASM, B = BENIGN, M = MALIGNANT, @PN = PRE-NEOPLASTIC

MICRO+ indicates histologic confirmation of preceding gross diagnosis.

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

NONPERFUSED				
GROUP:	0 PPM	FEMALE		

ANIMAL	800	11-MAR-94	STUDY DAY 12	
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE				
GROSS: NOT EXAMINED				
MICRO: NOT EXAMINED				
ANIMAL	764	12-MAR-94	STUDY DAY 13	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS.(G)	REL.	LYMPH ND, S-MAN	
LIVER	4.978	3.744	GROSS: SIZE INCREASE	
KIDNEYS	1.132	0.851	SLIGHT	
LUNGS	0.798	0.600	MICRO+((3)) PLASMACYTOSIS	
SPLEEN	0.413	0.311	MICRO: (3) SINUS ERYTHROCYTOSIS	
HEART	0.493	0.371	KIDNEYS	
BRAIN	1.633	1.228	MICRO: ((1)) MINERALIZATION	
ADRENAL GL	0.041	0.031	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
OVARIES	0.071	0.053	HEART	ORAL/PHARYNGEAL STOMACH
TERMINAL BODY WT.	133.0		LIVER	ADRENAL GL SPLEEN
			BRAIN	SPINAL CORD NERVE, SCIATIC
			NASAL CAVITY	LARYNX TRACHEA
			LUNGS	URINARY BLADDER
ANIMAL	803	12-MAR-94	STUDY DAY 13	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS.(G)	REL.	LYMPH ND, S-MAN	
LIVER	5.204	3.833	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL	
KIDNEYS	1.068	0.787	SEVERAL NODES, RED AND TAN	
LUNGS	0.928	0.684	MICRO+((3)) SINUS ERYTHROCYTOSIS	
SPLEEN	0.425	0.313	LYMPH ND, OTHER	
HEART	0.530	0.390	GROSS: SIZE INCREASE	
BRAIN	1.648	1.214	5X3X1 MM, DARK RED, LEFT RENAL	
ADRENAL GL	0.048	0.035	MICRO: 4 SINUS ERYTHROCYTOSIS	
OVARIES	0.095	0.070	THYMIC REGION	
TERMINAL BODY WT.	135.8		GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL	
			RED FOCAL AREAS	
			MICRO+((3)) HEMORRHAGE	
			BRAIN	
			MICRO: (2) BRAIN HEMORRHAGE	
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
			HEART	ORAL/PHARYNGEAL STOMACH
			LIVER	ADRENAL GL SPLEEN
			SPINAL CORD	NERVE, SCIATIC NASAL CAVITY
			LARYNX	TRACHEA LUNGS
			KIDNEYS	URINARY BLADDER
ANIMAL	801	11-MAR-94	STUDY DAY 12	
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE				
GROSS: NOT EXAMINED				
MICRO: NOT EXAMINED				
ANIMAL	784	12-MAR-94	STUDY DAY 13	
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS.(G)	REL.	SKIN	

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 PPM FEMALE			NONPERFUSED	
ANIMAL 784 (CONTINUED)				
LIVER	5.287	3.723	GROSS:	SWOLLEN
KIDNEYS	1.150	0.810		SLIGHT, PERIOcular TISSUE, BILATERAL
LUNGS	0.831	0.585	THYMIC REGION	
SPLEEN	0.407	0.287	GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
HEART	0.565*	0.398		LIGHT RED FOCAL AREAS
BRAIN	1.708	1.203	BRAIN	
ADRENAL GL	0.051	0.036	MICRO: (1)	VACUOLATION/SPONGIOSIS
OVARIES	0.093	0.065		OPTIC CHIASM, POSSIBLE PRESSURE
TERMINAL BODY WT.	142.0			ARTIFACT
			LARYNX	
			MICRO: 2	LARYNGITIS
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
			HEART	ORAL/PHARYNGEAL STOMACH
			LIVER	ADRENAL GL SKIN
			SPLEEN	THYMIC REGION SPINAL CORD
			NERVE, SCIATIC	NASAL CAVITY TRACHEA
			LUNGS	KIDNEYS URINARY BLADDER
ANIMAL 783 12-MAR-94 STUDY DAY 13				
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.		
LIVER	5.429	4.032	LIVER	
KIDNEYS	1.034	0.768	MICRO: (1)	MONONUCLEAR CELL INFILTRATE(S)
LUNGS	0.880	0.654	LYMPH ND, S-MAN	
SPLEEN	0.429	0.319	GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
HEART	0.574	0.426		ALL NODES, RED AND TAN
BRAIN	1.601	1.189	MICRO+((3))	SINUS ERYTHROCYTOSIS
ADRENAL GL	0.041	0.030	THYMIC REGION	
OVARIES	0.105	0.078	GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
TERMINAL BODY WT.	134.6			LIGHT RED FOCAL AREAS
			MICRO+((3))	HEMORRHAGE
			BRAIN	
			GROSS:	MENINGEAL HEMORRHAGE
				MODERATE
			LARYNX	
			MICRO: 2	ASPIRATED BLOOD
			TRACHEA	
			MICRO: 2	ASPIRATED BLOOD
			LUNGS	
			GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL
				RED FOCI, RIGHT APICAL AND LEFT LOBES
			MICRO: (2)	ALVEOLAR HISTIOCYTOSIS
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
			HEART	ORAL/PHARYNGEAL STOMACH
			ADRENAL GL	SPLEEN BRAIN
			SPINAL CORD	NERVE, SCIATIC NASAL CAVITY
			KIDNEYS	URINARY BLADDER
ANIMAL 778 12-MAR-94 STUDY DAY 13				
TYPE OF DEATH: SCHEDULED SACRIFICE				
ORGAN WEIGHT	ABS. (G)	REL.		
LIVER	5.524	3.806	LYMPH ND, S-MAN	
KIDNEYS	1.160	0.799	GROSS:	COLOR CHANGE, DIFFUSE
LUNGS	0.794	0.547		ONE NODE, DARK RED
SPLEEN	0.377	0.260	MICRO+((3))	SINUS ERYTHROCYTOSIS
			THYMIC REGION	

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	FEMALE	NONPERFUSED
<u>ANIMAL</u>	<u>778 (CONTINUED)</u>		
HEART	0.526	0.362	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
BRAIN	1.692	1.166	LIGHT RED FOCAL AREAS
ADRENAL GL	0.046	0.032	MICRO+ (2) HEMORRHAGE
OVARIES	0.100	0.069	LUNGS
TERMINAL BODY WT.	145.1		MICRO: (1) INTERSTITIAL PNEUMONITIS
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART ORAL/PHARYNGEAL STOMACH
			LIVER ADRENAL GL SPLEEN
			BRAIN SPINAL CORD NERVE, SCIATIC
			NASAL CAVITY LARYNX TRACHEA
			KIDNEYS URINARY BLADDER
<u>ANIMAL</u>	<u>777</u>	<u>11-MAR-94</u>	<u>STUDY DAY 12</u>
<u>TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE</u>			
			GROSS: NOT EXAMINED
			MICRO: NOT EXAMINED
<u>ANIMAL</u>	<u>775</u>	<u>11-MAR-94</u>	<u>STUDY DAY 12</u>
<u>TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE</u>			
			GROSS: NOT EXAMINED
			MICRO: NOT EXAMINED
<u>ANIMAL</u>	<u>809</u>	<u>11-MAR-94</u>	<u>STUDY DAY 12</u>
<u>TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE</u>			
			GROSS: NOT EXAMINED
			MICRO: NOT EXAMINED

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 100 PPM FEMALE NONPERFUSED

ANIMAL 797 11-MAR-94 STUDY DAY 12

TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE

GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

ANIMAL 810 11-MAR-94 STUDY DAY 12

TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE

GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

ANIMAL 793 12-MAR-94 STUDY DAY 13

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	5.204	3.993
KIDNEYS	1.114	0.855
LUNGS	0.800	0.614
SPLEEN	0.366	0.281
HEART	0.520	0.399
BRAIN	1.628	1.249
ADRENAL GL	0.053	0.041
OVARIES	0.079	0.061
TERMINAL BODY WT.	130.3	

LIVER
GROSS: ANOMALY
MEDIAN LOBES, NEAR HILUS, 9X5X3 MM
LYMPH ND, S-MAN
GROSS: COLOR CHANGE, DIFFUSE
ONE NODE ON THE LEFT SIDE
SPINAL CORD
MICRO: (P) EPIDERMAL INCLUSION CYST
DORSAL LUMBAR CORD
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
BRAIN

ANIMAL 789 12-MAR-94 STUDY DAY 13

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	5.898	4.175
KIDNEYS	1.167	0.826
LUNGS	0.882	0.624
SPLEEN	0.484	0.343
HEART	0.588	0.416
BRAIN	1.714	1.213
ADRENAL GL	0.056	0.040
OVARIES	0.095	0.067
TERMINAL BODY WT.	141.3	

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
BRAIN SPINAL CORD

ANIMAL 780 12-MAR-94 STUDY DAY 13

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	5.653	4.219
KIDNEYS	1.180	0.881
LUNGS	0.805	0.601
SPLEEN	0.407	0.304
HEART	0.544	0.406
BRAIN	1.675	1.250
ADRENAL GL	0.046	0.034
OVARIES	0.112	0.084
TERMINAL BODY WT.	134.0	

SKIN
GROSS: CRUST/SCAB/SCALE
RED CRUST, MILD, LEFT PERIOCLAR
REGION
LYMPH ND, S-MAN
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
SEVERAL NODES, RED AND TAN
THYMIC REGION
GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
RED FOCAL AREAS
BRAIN
MICRO: ((2)) MENINGEAL HEMORRHAGE
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
SPINAL CORD

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 100 PPM FEMALE NONPERFUSED

ANIMAL 779 12-MAR-94 STUDY DAY 13
TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL. SKIN
LIVER 5.784 4.000 GROSS: SWOLLEN
KIDNEYS 1.236 0.855 RIGHT PERIOCLAR AREA, MILD
LUNGS 0.793 0.548 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
SPLEEN 0.412 0.285 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
HEART 0.594 0.411 BRAIN SPINAL CORD
BRAIN 1.666 1.152
ADRENAL GL 0.045 0.031
OVARIES 0.112 0.077
TERMINAL BODY WT. 144.6

ANIMAL 807 11-MAR-94 STUDY DAY 12
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE
GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

ANIMAL 785 11-MAR-94 STUDY DAY 12
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE
GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

ANIMAL 772 12-MAR-94 STUDY DAY 13
TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL. LYMPH ND, S-MAN
LIVER 6.238 4.267 GROSS: COLOR CHANGE, DIFFUSE
KIDNEYS 1.260 0.862 ONE NODE IS RED
LUNGS 0.853 0.583 THYMIC REGION
SPLEEN 0.464 0.317 GROSS: COLOR CHANGE, FOCAL/MULTIFOAL
HEART 0.577 0.395 SEVERAL LIGHT RED 2 MM FOCI ON THE
BRAIN 1.741 1.191 LEFT SIDE
ADRENAL GL 0.051 0.035 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
OVARIES 0.109 0.075 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
TERMINAL BODY WT. 146.2 BRAIN SPINAL CORD

ANIMAL 799 11-MAR-94 STUDY DAY 12
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE
GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 500 PPM		FEMALE		NONPERFUSED	
ANIMAL	770	12-MAR-94	STUDY DAY	13	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	LYMPH ND, S-MAN		
LIVER	5.752	4.472	GROSS: COLOR CHANGE, DIFFUSE		
KIDNEYS	1.209	0.940	SEVERAL NODES, LIGHT RED		
LUNGS	0.863	0.671	MICRO: EXAMINED - NO SIGNIFICANT LESIONS		
SPLEEN	0.422	0.328	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
HEART	0.528	0.411	BRAIN SPINAL CORD		
BRAIN	1.650	1.283			
ADRENAL GL	0.043	0.033			
OVARIES	0.093	0.072			
TERMINAL BODY WT.	128.6				
ANIMAL	805	12-MAR-94	STUDY DAY	13	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	SKIN		
LIVER	6.313	4.456	GROSS: CRUST/SCAB/SCALE		
KIDNEYS	1.224	0.864	RED CRUST, RIGHT PERIOCLAR AREA		
LUNGS	0.913	0.644	EYE		
SPLEEN	0.442	0.312	GROSS: TRAUMATIZED		
HEART	0.609	0.430	RIGHT, DUE TO BLEEDING		
BRAIN	1.642	1.159	MICRO: EXAMINED - NO SIGNIFICANT LESIONS		
ADRENAL GL	0.049	0.035	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
OVARIES	0.119	0.084	BRAIN SPINAL CORD		
TERMINAL BODY WT.	141.7				
ANIMAL	788	11-MAR-94	STUDY DAY	12	
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE					
GROSS: NOT EXAMINED					
MICRO: NOT EXAMINED					
ANIMAL	806	12-MAR-94	STUDY DAY	13	
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.	LYMPH ND, S-MAN		
LIVER	6.229	4.452	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL		
KIDNEYS	1.159	0.828	TAN AND RED		
LUNGS	0.756	0.540	THYMIC REGION		
SPLEEN	0.463	0.331	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL		
HEART	0.578	0.413	MULTIPLE RED FOCAL AREAS		
BRAIN	1.628	1.164	MICRO: EXAMINED - NO SIGNIFICANT LESIONS		
ADRENAL GL	0.036	0.026	THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
OVARIES	0.082	0.059	BRAIN SPINAL CORD		
TERMINAL BODY WT.	139.9				
ANIMAL	808	11-MAR-94	STUDY DAY	12	
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE					
GROSS: NOT EXAMINED					
MICRO: NOT EXAMINED					

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 500 PPM FEMALE NONPERFUSED

ANIMAL 762 11-MAR-94 STUDY DAY 12
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE
GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

ANIMAL 781 12-MAR-94 STUDY DAY 13
TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL. THYMIC REGION
LIVER 6.039 4.453 GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
KIDNEYS 1.186 0.875 SEVERAL DARK RED 1 MM FOCI ON THE
LUNGS 0.812 0.599 POSTERIOR EDGE, THE FOCI
SPLEEN 0.424 0.313 ARE ON A LIGHT RED BACKGROUND
HEART 0.576 0.425 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
BRAIN 1.678 1.237 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
ADRENAL GL 0.049 0.036 BRAIN SPINAL CORD
OVARIES 0.102 0.075
TERMINAL BODY WT. 135.6

ANIMAL 771 11-MAR-94 STUDY DAY 12
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE
GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

ANIMAL 774 12-MAR-94 STUDY DAY 13
TYPE OF DEATH: SCHEDULED SACRIFICE
ORGAN WEIGHT ABS.(G) REL. LYMPH ND, S-MAN
LIVER 6.133 4.530 GROSS: COLOR CHANGE, DIFFUSE
KIDNEYS 1.168 0.863 RED
LUNGS 0.873 0.645 EYE
SPLEEN 0.424 0.313 GROSS: TRAUMATIZED
HEART 0.543 0.401 RIGHT, DUE TO BLEEDING
BRAIN 1.692 1.250 MICRO: EXAMINED - NO SIGNIFICANT LESIONS
ADRENAL GL 0.049 0.036 THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
OVARIES 0.102 0.075 BRAIN SPINAL CORD
TERMINAL BODY WT. 135.4

ANIMAL 776 11-MAR-94 STUDY DAY 12
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE
GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

NONPERFUSED			
GROUP:	1000 PPM	FEMALE	
ANIMAL	791	11-MAR-94	STUDY DAY 12
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE			
GROSS: NOT EXAMINED			
MICRO: NOT EXAMINED			
ANIMAL	773	12-MAR-94	STUDY DAY 13
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	SKIN
LIVER	5.533	4.653	GROSS: CRUST/SCAB/SCALE
KIDNEYS	1.105	0.929	RED CRUST, PERINASAL AREA
LUNGS	0.745	0.627	LYMPH ND, S-MAN
SPLEEN	0.299	0.251	GROSS: COLOR CHANGE, FOCAL/MULTIFOCAL
HEART	0.660	0.555	TAN AND RED
BRAIN	1.550	1.304	MICRO+ (2) SINUS ERYTHROCYTOSIS
ADRENAL GL	0.056	0.047	MICRO: ((3)) CYSTIC LYMPHATIC ECTASIA
OVARIES	0.086	0.072	BRAIN
TERMINAL BODY WT.	118.9		MICRO: ((2)) VACUOLATION/SPONGIOSIS
			BRAINSTEM
			SPINAL CORD
			MICRO: ((2)) VACUOLATION/SPONGIOSIS
			EYE
			GROSS: TRAUMATIZED
			LEFT, DUE TO BLEEDING
			MICRO+ (2) RETROORBITAL HEMORRHAGE
			HARDERIAN GL
			GROSS: COLOR CHANGE, DIFFUSE
			LEFT, DARK RED
			MICRO: (2) FIBROSIS
			LUNGS
			MICRO: (2) HEMORRHAGE
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			HEART ORAL/PHARYNGEAL STOMACH
			LIVER ADRENAL GL SKIN
			SPLEEN NERVE, SCIATIC NASAL CAVITY
			LARYNX TRACHEA KIDNEYS
			URINARY BLADDER
ANIMAL	782	12-MAR-94	STUDY DAY 13
TYPE OF DEATH: SCHEDULED SACRIFICE			
ORGAN WEIGHT	ABS. (G)	REL.	SKIN
LIVER	6.438	5.348	GROSS: SWOLLEN
KIDNEYS	1.082	0.899	MILD, PERIOCLULAR TISSUE, BILATERAL
LUNGS	0.782	0.650	SKIN
SPLEEN	0.464	0.385	GROSS: CRUST/SCAB/SCALE
HEART	0.552	0.459	RIGHT PERIOCLULAR TISSUE, MILD
BRAIN	1.479	1.229	BROWN, PERINASAL REGION
ADRENAL GL	0.041	0.034	LYMPH ND, S-MAN
OVARIES	0.087	0.072	GROSS: COLOR CHANGE, DIFFUSE
TERMINAL BODY WT.	120.4		SEVERAL NODES, LIGHT RED
			MICRO+ (3) SINUS ERYTHROCYTOSIS
			BRAIN
			MICRO: ((3)) MENINGEAL HEMORRHAGE
			LATERAL AND 3RD VENTRICLES

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 PPM FEMALE NONPERFUSED

ANIMAL 782 (CONTINUED)

((2)) VACUOLATION/SPONGIOSIS
BRAINSTEM AND VESTIBULAR NUCLEI
SPINAL CORD
MICRO: ((3)) VACUOLATION/SPONGIOSIS
OVARIES
GROSS: CYST
1 MM DIAMETER, RIGHT
NASAL CAVITY
MICRO: (2) RHINITIS
KIDNEYS
MICRO: ((1)) MINERALIZATION
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
HEART ORAL/PHARYNGEAL STOMACH
LIVER ADRENAL GL SKIN
SPLEEN NERVE, SCIATIC OVARIES
LARYNX TRACHEA LUNGS
URINARY BLADDER

ANIMAL 795 12-MAR-94 STUDY DAY 13

TYPE OF DEATH: SCHEDULED SACRIFICE

ORGAN WEIGHT	ABS.(G)	REL.
LIVER	6.280	4.897
KIDNEYS	1.169	0.912
LUNGS	0.832	0.649
SPLEEN	0.335	0.261
HEART	0.527	0.411
BRAIN	1.556	1.213
ADRENAL GL	0.043	0.034
OVARIES	0.076	0.059
TERMINAL BODY WT.	128.3	

SKIN
GROSS: CRUST/SCAB/SCALE
RED CRUST, LEFT PERIOcular AREA
BRAIN
MICRO: ((2)) VACUOLATION/SPONGIOSIS
BRAINSTEM
SPINAL CORD
MICRO: ((3)) VACUOLATION/SPONGIOSIS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
HEART ORAL/PHARYNGEAL STOMACH
LIVER ADRENAL GL SKIN
SPLEEN NERVE, SCIATIC NASAL CAVITY
LARYNX TRACHEA LUNGS
KIDNEYS URINARY BLADDER

ANIMAL 794 11-MAR-94 STUDY DAY 12

TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE

GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

ANIMAL 786 11-MAR-94 STUDY DAY 12

TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE

GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

ANIMAL 767 11-MAR-94 STUDY DAY 12

TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE

GROSS: NOT EXAMINED
MICRO: NOT EXAMINED

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 4
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 PPM		FEMALE		NONPERFUSED	

ANIMAL	765	12-MAR-94	STUDY DAY 13		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.			
LIVER	6.777	5.112	ORAL/PHARYNGEAL		
KIDNEYS	1.143	0.862	MICRO: ((4))	HEMORRHAGE	
LUNGS	0.874	0.659		SOFT TISSUE OF FACE	
SPLEEN	0.409	0.309	SKIN		
HEART	0.554	0.418	GROSS:	SWOLLEN	
BRAIN	1.652	1.246		PERIOCLAR TISSUE, BILATERAL	
ADRENAL GL	0.049	0.037	SKIN		
OVARIES	0.099	0.075	GROSS:	CRUST/SCAB/SCALE	
TERMINAL BODY WT.	132.6			RED, LEFT PERIOCLAR REGION, MILD	
			LYMPH ND, S-MAN		
			GROSS:	COLOR CHANGE, DIFFUSE	
				SEVERAL NODES, RED	
			MICRO+((3))	SINUS ERYTHROCYTOSIS	
			BRAIN		
			MICRO: ((2))	VACUOLATION/SPONGIOSIS	
				BRAINSTEM	
			SPINAL CORD		
			MICRO: ((4))	VACUOLATION/SPONGIOSIS	
			LUNGS		
			MICRO: ((1))	ALVEOLAR HISTIOCYTOSIS	
			KIDNEYS		
			MICRO: (1)	MINERALIZATION	
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
			HEART	STOMACH	LIVER
			ADRENAL GL	SKIN	SPLEEN
			NERVE, SCIATIC	NASAL CAVITY	LARYNX
			TRACHEA	URINARY BLADDER	
ANIMAL	768	11-MAR-94	STUDY DAY 12		
TYPE OF DEATH: SCHEDULED PERFUSION SACRIFICE					
			GROSS:	NOT EXAMINED	
			MICRO:	NOT EXAMINED	
ANIMAL	787	12-MAR-94	STUDY DAY 13		
TYPE OF DEATH: SCHEDULED SACRIFICE					
ORGAN WEIGHT	ABS.(G)	REL.			
LIVER	7.042	5.049	SKIN		
KIDNEYS	1.220	0.875	GROSS:	CRUST/SCAB/SCALE	
LUNGS	0.820	0.588		RED CRUST, PERINASAL AND LEFT	
SPLEEN	0.362	0.260		PERIOCLAR AREA	
HEART	0.565	0.405	LYMPH ND, S-MAN		
BRAIN	1.623	1.164	GROSS:	COLOR CHANGE, FOCAL/MULTIFOCAL	
ADRENAL GL	0.050	0.036		TAN AND RED	
OVARIES	0.124	0.089	MICRO+((3))	SINUS ERYTHROCYTOSIS	
TERMINAL BODY WT.	139.5		BRAIN		
			MICRO: ((2))	VACUOLATION/SPONGIOSIS	
				BRAINSTEM	
			SPINAL CORD		
			MICRO: ((3))	VACUOLATION/SPONGIOSIS	
			NASAL CAVITY		
			MICRO: ((2))	HEMORRHAGE	
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:		
			HEART	ORAL/PHARYNGEAL	STOMACH
			LIVER	ADRENAL GL	SKIN
			SPLEEN	NERVE, SCIATIC	LARYNX
			TRACHEA	LUNGS	KIDNEYS
			URINARY BLADDER		

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

NMOD_RPT:VPTRF.TB4/CM/013095

TABLE 5
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

NECROPSY PROTOCOL

PERFUSED MALES

The following tissues were examined at necropsy with no significant lesions observed unless specified on individual animal page:

BRAIN, NOS	SPINAL CORD, CRV	SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE	PERONEAL/SURAL N
TAIL				

The microscopic procedures used in this study are described in the methods section of the text.

Micro diagnosis grade codes:

1=MINIMAL, 2=MILD, 3=MODERATE, 4=MARKED, 5=SEVERE, P=PRESENT

Micro diagnosis distribution codes:

()=FOCAL, (())=MULTIFOCAL, NO PARENTHESES=DIFFUSE

Micro diagnosis prefix codes:

= NEOPLASM, B = BENIGN, M = MALIGNANT, @PN = PRE-NEOPLASTIC

MICRO+ indicates histologic confirmation of preceding gross diagnosis.

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	MALE	PERFUSED
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ANIMAL 717 10-MAR-94

TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS

FRONTAL CORTEX
MICRO: MICROSCOPICALLY NORMAL
FREEZE ARTIFACT

OCCIPITAL CORTEX
MICRO: MICROSCOPICALLY NORMAL
SEVERE FREEZE ARTIFACT

SEPTAL NUCLEI
MICRO: MICROSCOPICALLY NORMAL
FREEZE ARTIFACT

CAUD NUC/PUTAMEN
MICRO: MICROSCOPICALLY NORMAL
SEVERE FREEZE ARTIFACT

GLOBUS PALLIDUS
MICRO: MICROSCOPICALLY NORMAL
SEVERE FREEZE ARTIFACT

HIPPOCAMPUS
MICRO: MICROSCOPICALLY NORMAL
SEVERE FREEZE ARTIFACT

THALAMUS
MICRO: MICROSCOPICALLY NORMAL
SEVERE FREEZE ARTIFACT PRECLUDES A
GOOD EXAMINATION

HYPOTHALAMUS
MICRO: MICROSCOPICALLY NORMAL
SEVERE FREEZE ARTIFACT PRECLUDES A
GOOD EXAM

MIDBRAIN
MICRO: MICROSCOPICALLY NORMAL
SEVERE FREEZE ARTIFACT

CEREBELLAR NUC
MICRO: MICROSCOPICALLY NORMAL
SEVERE FREEZE ARTIFACT

VESTIBULAR NUC
MICRO: MICROSCOPICALLY NORMAL
SEVERE FREEZE ARTIFACT

PONS
MICRO: MICROSCOPICALLY NORMAL
SEVERE FREEZE ARTIFACT PRECLUDES A
GOOD EXAM

MEDULLA OBL
MICRO: MICROSCOPICALLY NORMAL
SEVERE FREEZE ARTIFACT

SPINAL CORD, CRV
MICRO: MICROSCOPICALLY NORMAL
FREEZE ARTIFACT

SPINAL CORD, THR
MICRO: MICROSCOPICALLY NORMAL
FREEZE ARTIFACT

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA

See necropsy protocol page for list of tissues examined grossly and for explanation of grades

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	MALE	PERFUSED
<u>ANIMAL</u>	<u>717 (CONTINUED)</u>		
			Cerebellar W.M. ANT COMMISSURE EXTERNAL CAPSULE INTERNAL CAPSULE CORPUS CALLOSUM CEREBELLAR CTX CEREBELLAR NUC VESTIBULAR NUC PONS MEDULLA OBL OLFACTORY BULB OPTIC N/CHIASM TRIGEMINAL TRACT SPINAL CORD, CRV SPINAL CORD, THR SPINAL CORD, LUM SPINAL NERVE RTS DORSAL ROOT GANG GASSERIAN GANG SCIATIC NERVE TIBIAL NERVE PERONEAL/SURAL N THE FOLLOWING TISSUES WERE MISSING: FORNIX
<u>ANIMAL</u>	<u>715</u>	<u>10-MAR-94</u>	
			TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION GROSS: EXAMINED - NO SIGNIFICANT LESIONS GASSERIAN GANG MICRO: (2) HEMORRHAGE THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL: MENINGES PIRIFORM CORTEX FRONTAL CORTEX PARIETAL CORTEX TEMPORAL CORTEX OCCIPITAL CORTEX SEPTAL NUCLEI CAUD NUC/PUTAMEN GLOBUS PALLIDUS AMYGDALA HIPPOCAMPUS THALAMUS HYPOTHALAMUS MIDBRAIN SUBSTANTIA NIGRA CEREBELLAR W.M. ANT COMMISSURE EXTERNAL CAPSULE INTERNAL CAPSULE CORPUS CALLOSUM FORNIX CEREBELLAR CTX CEREBELLAR NUC VESTIBULAR NUC PONS MEDULLA OBL OLFACTORY BULB OPTIC N/CHIASM TRIGEMINAL TRACT SPINAL CORD, CRV SPINAL CORD, THR SPINAL CORD, LUM SPINAL NERVE RTS DORSAL ROOT GANG SCIATIC NERVE TIBIAL NERVE PERONEAL/SURAL N
<u>ANIMAL</u>	<u>750</u>	<u>10-MAR-94</u>	
			TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION GROSS: EXAMINED - NO SIGNIFICANT LESIONS SPINAL CORD, CRV MICRO: MICROSCOPICALLY NORMAL MODERATE FREEZE ARTIFACT SPINAL CORD, THR MICRO: MICROSCOPICALLY NORMAL MODERATE FREEZE ARTIFACT SPINAL CORD, LUM MICRO: MICROSCOPICALLY NORMAL MODERATE FREEZE ARTIFACT THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL: MENINGES PIRIFORM CORTEX FRONTAL CORTEX PARIETAL CORTEX TEMPORAL CORTEX OCCIPITAL CORTEX SEPTAL NUCLEI CAUD NUC/PUTAMEN GLOBUS PALLIDUS AMYGDALA HIPPOCAMPUS THALAMUS HYPOTHALAMUS MIDBRAIN SUBSTANTIA NIGRA CEREBELLAR W.M. ANT COMMISSURE EXTERNAL CAPSULE INTERNAL CAPSULE CORPUS CALLOSUM CEREBELLAR CTX CEREBELLAR NUC VESTIBULAR NUC PONS MEDULLA OBL OLFACTORY BULB OPTIC N/CHIASM TRIGEMINAL TRACT SPINAL CORD, CRV SPINAL CORD, THR SPINAL CORD, LUM SPINAL NERVE RTS DORSAL ROOT GANG GASSERIAN GANG SCIATIC NERVE TIBIAL NERVE

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 PPM

MALE

PERFUSED

ANIMAL 750 (CONTINUED)

PERONEAL/SURAL N

THE FOLLOWING TISSUES WERE MISSING:

FORNIX

ANIMAL 751 10-MAR-94

TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS

CAUD NUC/PUTAMEN

MICRO: MICROSCOPICALLY NORMAL

MILD FREEZE ARTIFACT IN MANY AREAS OF THE BRAIN

SPINAL CORD, CRV

MICRO: MICROSCOPICALLY NORMAL

MODERATE FREEZE ARTIFACT IN CERVICAL AND THORACIC SECTIONS

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES

PIRIFORM CORTEX

FRONTAL CORTEX

PARIETAL CORTEX

TEMPORAL CORTEX

OCCIPITAL CORTEX

CAUD NUC/PUTAMEN

GLOBUS PALLIDUS

AMYGDALA

HIPPOCAMPUS

THALAMUS

HYPOTHALAMUS

MIDBRAIN

SUBSTANTIA NIGRA

CEREBELLAR W.M.

ANT COMMISSURE

EXTERNAL CAPSULE

INTERNAL CAPSULE

CORPUS CALLOSUM

FORNIX

CEREBELLAR CTX

CEREBELLAR NUC

VESTIBULAR NUC

PONS

MEDULLA OBL

OLFACTORY BULB

OPTIC N/CHIASM

TRIGEMINAL TRACT

SPINAL CORD, CRV

SPINAL CORD, THR

SPINAL CORD, LUM

SPINAL NERVE RTS

DORSAL ROOT GANG

GASSERIAN GANG

SCIATIC NERVE

TIBIAL NERVE

PERONEAL/SURAL N

THE FOLLOWING TISSUES WERE MISSING:

SEPTAL NUCLEI

ANIMAL 738 10-MAR-94

TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS

SPINAL CORD, CRV

MICRO: ((1)) VACUOLATION

DORSAL WHITE MATTER FOCUS

SPINAL CORD, THR

MICRO: ((1)) VACUOLATION

DORSAL AND LATERAL FOCI

SPINAL CORD, LUM

MICRO: (1) VACUOLATION

SINGLE DORSAL FOCUS

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES

PIRIFORM CORTEX

FRONTAL CORTEX

PARIETAL CORTEX

TEMPORAL CORTEX

OCCIPITAL CORTEX

SEPTAL NUCLEI

CAUD NUC/PUTAMEN

GLOBUS PALLIDUS

AMYGDALA

HIPPOCAMPUS

THALAMUS

HYPOTHALAMUS

MIDBRAIN

SUBSTANTIA NIGRA

CEREBELLAR W.M.

ANT COMMISSURE

EXTERNAL CAPSULE

INTERNAL CAPSULE

CORPUS CALLOSUM

FORNIX

CEREBELLAR CTX

CEREBELLAR NUC

VESTIBULAR NUC

PONS

MEDULLA OBL

OLFACTORY BULB

OPTIC N/CHIASM

TRIGEMINAL TRACT

SPINAL NERVE RTS

DORSAL ROOT GANG

GASSERIAN GANG

SCIATIC NERVE

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	MALE	PERFUSED
<u>ANIMAL</u>	<u>738 (CONTINUED)</u>		
		TIBIAL NERVE	PERONEAL/SURAL N

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

			PERFUSED
GROUP:	100 PPM	MALE	
<hr/>			
ANIMAL	745	10-MAR-94	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			
GROSS: EXAMINED - NO SIGNIFICANT LESIONS			
MICRO: EXAMINED - NO SIGNIFICANT LESIONS			
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX	
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX	
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	
AMYGDALA	HIPPOCAMPUS	THALAMUS	
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA	
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE	
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX	
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC	
PONS	OLFACTORY BULB	OPTIC N/CHIASM	
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR	
SPINAL CORD, LUM			
THE FOLLOWING TISSUES WERE MISSING:			
MEDULLA OBL			
ANIMAL	703	10-MAR-94	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			
GROSS: EXAMINED - NO SIGNIFICANT LESIONS			
MICRO: EXAMINED - NO SIGNIFICANT LESIONS			
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX	
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX	
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	
AMYGDALA	HIPPOCAMPUS	THALAMUS	
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA	
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE	
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX	
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC	
PONS	MEDULLA OBL	OLFACTORY BULB	
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV	
SPINAL CORD, THR	SPINAL CORD, LUM		
THE FOLLOWING TISSUES WERE MISSING:			
OPTIC N/CHIASM			
ANIMAL	709	10-MAR-94	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			
GROSS: EXAMINED - NO SIGNIFICANT LESIONS			
MICRO: EXAMINED - NO SIGNIFICANT LESIONS			
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX	
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX	
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	
AMYGDALA	HIPPOCAMPUS	THALAMUS	
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA	
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE	
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX	
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC	
PONS	MEDULLA OBL	OLFACTORY BULB	
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR	
SPINAL CORD, LUM			
THE FOLLOWING TISSUES WERE MISSING:			
OPTIC N/CHIASM			

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 100 PPM MALE PERFUSED

ANIMAL 755 10-MAR-94

TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
MENINGES PIRIFORM CORTEX FRONTAL CORTEX
PARIETAL CORTEX TEMPORAL CORTEX OCCIPITAL CORTEX
SEPTAL NUCLEI CAUD NUC/PUTAMEN GLOBUS PALLIDUS
AMYGDALA HIPPOCAMPUS THALAMUS
HYPOTHALAMUS MIDBRAIN SUBSTANTIA NIGRA
CEREBELLAR W.M. ANT COMMISSURE EXTERNAL CAPSULE
INTERNAL CAPSULE CORPUS CALLOSUM FORNIX
CEREBELLAR CTX CEREBELLAR NUC VESTIBULAR NUC
PONS MEDULLA OBL OLFACTORY BULB
OPTIC N/CHIASM TRIGEMINAL TRACT SPINAL CORD, CRV
SPINAL CORD, THR SPINAL CORD, LUM

ANIMAL 719 10-MAR-94

TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
MENINGES PIRIFORM CORTEX FRONTAL CORTEX
PARIETAL CORTEX TEMPORAL CORTEX OCCIPITAL CORTEX
SEPTAL NUCLEI CAUD NUC/PUTAMEN GLOBUS PALLIDUS
AMYGDALA HIPPOCAMPUS THALAMUS
HYPOTHALAMUS MIDBRAIN SUBSTANTIA NIGRA
CEREBELLAR W.M. ANT COMMISSURE EXTERNAL CAPSULE
INTERNAL CAPSULE CORPUS CALLOSUM FORNIX
CEREBELLAR CTX CEREBELLAR NUC VESTIBULAR NUC
PONS MEDULLA OBL OLFACTORY BULB
TRIGEMINAL TRACT SPINAL CORD, CRV SPINAL CORD, THR
SPINAL CORD, LUM
THE FOLLOWING TISSUES WERE MISSING:
OPTIC N/CHIASM

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	500 PPM	MALE	PERFUSED
<hr/>			
<u>ANIMAL</u>	<u>743</u>	<u>10-MAR-94</u>	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			
GROSS: EXAMINED - NO SIGNIFICANT LESIONS			
MICRO: EXAMINED - NO SIGNIFICANT LESIONS			
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX	
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX	
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	
AMYGDALA	HIPPOCAMPUS	THALAMUS	
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA	
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE	
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX	
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC	
PONS	MEDULLA OBL	OLFACTORY BULB	
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV	
SPINAL CORD, THR	SPINAL CORD, LUM		
<u>ANIMAL</u>	<u>710</u>	<u>10-MAR-94</u>	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			
GROSS: EXAMINED - NO SIGNIFICANT LESIONS			
MICRO: EXAMINED - NO SIGNIFICANT LESIONS			
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX	
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX	
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	
AMYGDALA	HIPPOCAMPUS	THALAMUS	
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA	
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE	
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX	
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC	
PONS	MEDULLA OBL	OLFACTORY BULB	
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV	
SPINAL CORD, THR	SPINAL CORD, LUM		
<u>ANIMAL</u>	<u>731</u>	<u>10-MAR-94</u>	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			
SKIN			
GROSS: CRUST/SCAB/SCALE			
PERINASAL REGION, RED CRUST			
MICRO: EXAMINED - NO SIGNIFICANT LESIONS			
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX	
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX	
CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	AMYGDALA	
HIPPOCAMPUS	THALAMUS	HYPOTHALAMUS	
MIDBRAIN	SUBSTANTIA NIGRA	CEREBELLAR W.M.	
ANT COMMISSURE	EXTERNAL CAPSULE	INTERNAL CAPSULE	
CORPUS CALLOSUM	CEREBELLAR CTX	CEREBELLAR NUC	
VESTIBULAR NUC	PONS	MEDULLA OBL	
OLFACTORY BULB	OPTIC N/CHIASM	TRIGEMINAL TRACT	
SPINAL CORD, CRV	SPINAL CORD, THR	SPINAL CORD, LUM	
THE FOLLOWING TISSUES WERE MISSING:			
SEPTAL NUCLEI	FORNIX		

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	500 PPM	MALE	PERFUSED
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ANIMAL 722 10-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

EYE

GROSS: TRAUMATIZED
LEFT, DUE TO BLEEDING

MICRO: EXAMINED - NO SIGNIFICANT LESIONS

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX
CEREBELLAR NUC	VESTIBULAR NUC	PONS
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR
SPINAL CORD, LUM		

THE FOLLOWING TISSUES WERE MISSING:
FORNIX

ANIMAL 721 10-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS

CAUD NUC/PUTAMEN

MICRO: MICROSCOPICALLY NORMAL

FREEZE ARTIFACT PRESENT IN THE BRAIN

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	AMYGDALA
HIPPOCAMPUS	THALAMUS	HYPOTHALAMUS
MIDBRAIN	SUBSTANTIA NIGRA	CEREBELLAR W.M.
ANT COMMISSURE	EXTERNAL CAPSULE	INTERNAL CAPSULE
CORPUS CALLOSUM	CEREBELLAR CTX	CEREBELLAR NUC
VESTIBULAR NUC	PONS	MEDULLA OBL
OLFACTORY BULB	OPTIC N/CHIASM	TRIGEMINAL TRACT
SPINAL CORD, CRV	SPINAL CORD, THR	SPINAL CORD, LUM

THE FOLLOWING TISSUES WERE MISSING:
SEPTAL NUCLEI FORNIX

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 PPM MALE PERFUSED

ANIMAL 729 10-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
VESTIBULAR NUC
MICRO: ((2)) MYELINOPATHY
PONS
MICRO: ((3)) MYELINOPATHY
PRIMARILY IN THE MEDIAL LONGITUDINAL
FASCICULUS, WITH
SOME LESIONS MORE LATERAL
((3)) AXONOPATHY
MEDULLA OBL
MICRO: ((4)) MYELINOPATHY
VENTRAL WHITE MATTER TRACTS ONLY
SPINAL CORD, CRV
MICRO: ((4)) MYELINOPATHY
VENTRAL MOST SEVERE, LATERAL Milder,
DORSAL IS MINIMAL
ONLY WHITE MATTER TRACTS AFFECTED
((3)) AXONOPATHY
SPINAL CORD, THR
MICRO: ((4)) MYELINOPATHY
VENTRAL AND LATERAL WHITE MATTER BOTH
AFFECTED
((3)) AXONOPATHY
SPINAL CORD, LUM
MICRO: ((2)) MYELINOPATHY
VENTRAL AND LATERAL WHITE MATTER

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
MENINGES PIRIFORM CORTEX FRONTAL CORTEX
PARIETAL CORTEX TEMPORAL CORTEX OCCIPITAL CORTEX
CAUD NUC/PUTAMEN GLOBUS PALLIDUS AMYGDALA
HIPPOCAMPUS THALAMUS HYPOTHALAMUS
MIDBRAIN CEREBELLAR W.M. ANT COMMISSURE
EXTERNAL CAPSULE INTERNAL CAPSULE CORPUS CALLOSUM
CEREBELLAR CTX CEREBELLAR NUC OLFACTORY BULB
OPTIC N/CHIASM TRIGEMINAL TRACT SPINAL NERVE RTS
DORSAL ROOT GANG GASSERIAN GANG SCIATIC NERVE
TIBIAL NERVE PERONEAL/SURAL N

THE FOLLOWING TISSUES WERE MISSING:
SEPTAL NUCLEI SUBSTANTIA NIGRA FORNIX

ANIMAL 712 10-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MIDBRAIN
MICRO: ((1)) MYELINOPATHY
VESTIBULAR NUC
MICRO: ((2)) MYELINOPATHY
PONS
MICRO: ((3)) MYELINOPATHY
((3)) AXONOPATHY
MEDULLA OBL
MICRO: ((4)) MYELINOPATHY
((3)) AXONOPATHY
TRIGEMINAL TRACT

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	1000 PPM	MALE	PERFUSED
<u>ANIMAL</u>	<u>712 (CONTINUED)</u>		
			MICRO: ((1)) MYELINOPATHY ((1)) AXONOPATHY SPINAL CORD, CRV MICRO: ((4)) MYELINOPATHY ((3)) AXONOPATHY SPINAL CORD, THR MICRO: ((4)) MYELINOPATHY ((3)) AXONOPATHY SPINAL CORD, LUM MICRO: ((3)) MYELINOPATHY ((3)) AXONOPATHY THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL: MENINGES PIRIFORM CORTEX FRONTAL CORTEX PARIETAL CORTEX TEMPORAL CORTEX OCCIPITAL CORTEX SEPTAL NUCLEI CAUD NUC/PUTAMEN GLOBUS PALLIDUS AMYGDALA HIPPOCAMPUS THALAMUS HYPOTHALAMUS SUBSTANTIA NIGRA CEREBELLAR W.M. ANT COMMISSURE EXTERNAL CAPSULE INTERNAL CAPSULE CORPUS CALLOSUM CEREBELLAR CTX CEREBELLAR NUC OLFACTORY BULB OPTIC N/CHIASM SPINAL NERVE RTS DORSAL ROOT GANG GASSERIAN GANG SCIATIC NERVE TIBIAL NERVE PERONEAL/SURAL N THE FOLLOWING TISSUES WERE MISSING: FORNIX
<u>ANIMAL</u>	<u>727</u>	<u>10-MAR-94</u>	
TYPE OF DEATH: SCHEDULED SACRIFICE -	PERFUSION		
	MIDBRAIN		MICRO: ((2)) MYELINOPATHY WHITE MATTER, MEDIAL
	VESTIBULAR NUC		MICRO: ((2)) MYELINOPATHY
	PONS		MICRO: ((2)) MYELINOPATHY ((2)) AXONOPATHY
	MEDULLA OBL		MICRO: ((3)) MYELINOPATHY ((2)) AXONOPATHY
	SPINAL CORD, CRV		MICRO: ((4)) MYELINOPATHY ((3)) AXONOPATHY
	SPINAL CORD, THR		MICRO: ((3)) MYELINOPATHY ((3)) AXONOPATHY
	SPINAL CORD, LUM		MICRO: ((2)) MYELINOPATHY
	SKIN		GROSS: CRUST/SCAB/SCALE RED CRUST, PERIOcular TISSUE, BILATERAL
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL: MENINGES PIRIFORM CORTEX FRONTAL CORTEX PARIETAL CORTEX TEMPORAL CORTEX OCCIPITAL CORTEX CAUD NUC/PUTAMEN GLOBUS PALLIDUS AMYGDALA HIPPOCAMPUS THALAMUS HYPOTHALAMUS SUBSTANTIA NIGRA CEREBELLAR W.M. ANT COMMISSURE

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 PPM MALE PERFUSED

ANIMAL 727 (CONTINUED)
EXTERNAL CAPSULE INTERNAL CAPSULE CORPUS CALLOSUM
CEREBELLAR CTX CEREBELLAR NUC OLFACTORY BULB
OPTIC N/CHIASM TRIGEMINAL TRACT SPINAL NERVE RTS
DORSAL ROOT GANG GASSERIAN GANG SCIATIC NERVE
TIBIAL NERVE PERONEAL/SURAL N
THE FOLLOWING TISSUES WERE MISSING:
SEPTAL NUCLEI FORNIX

ANIMAL 739 10-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION
GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MIDBRAIN
MICRO: ((1)) MYELINOPATHY
PONS
MICRO: ((3)) MYELINOPATHY
((3)) AXONOPATHY
MEDULLA OBL
MICRO: ((3)) MYELINOPATHY
((3)) AXONOPATHY
TRIGEMINAL TRACT
MICRO: ((1)) MYELINOPATHY
SPINAL CORD, CRV
MICRO: ((4)) MYELINOPATHY
INVOLVES THE VENTRAL/LATERAL FUNICULI
((3)) AXONOPATHY
SPINAL CORD, THR
MICRO: ((4)) MYELINOPATHY
((3)) AXONOPATHY
SPINAL CORD, LUM
MICRO: ((3)) MYELINOPATHY
((2)) AXONOPATHY
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
MENINGES PIRIFORM CORTEX FRONTAL CORTEX
PARIETAL CORTEX TEMPORAL CORTEX OCCIPITAL CORTEX
SEPTAL NUCLEI CAUD NUC/PUTAMEN GLOBUS PALLIDUS
AMYGDALA HIPPOCAMPUS THALAMUS
HYPOTHALAMUS SUBSTANTIA NIGRA CEREBELLAR W.M.
ANT COMMISSURE EXTERNAL CAPSULE INTERNAL CAPSULE
CORPUS CALLOSUM CEREBELLAR CTX VESTIBULAR NUC
OLFACTORY BULB OPTIC N/CHIASM SPINAL NERVE RTS
DORSAL ROOT GANG GASSERIAN GANG SCIATIC NERVE
TIBIAL NERVE PERONEAL/SURAL N
THE FOLLOWING TISSUES WERE MISSING:
FORNIX CEREBELLAR NUC

ANIMAL 732 10-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION
VESTIBULAR NUC
MICRO: ((1)) MYELINOPATHY
PONS
MICRO: ((3)) MYELINOPATHY
((3)) AXONOPATHY
MEDULLA OBL
MICRO: ((3)) MYELINOPATHY

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 6
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	1000 PPM	MALE	PERFUSED
ANIMAL	732 (CONTINUED)		
			((3)) AXONOPATHY
		SPINAL CORD, CRV	
		MICRO: ((3)) MYELINOPATHY	
		((3)) AXONOPATHY	
		SPINAL CORD, THR	
		MICRO: ((3)) MYELINOPATHY	
		((3)) AXONOPATHY	
		SPINAL CORD, LUM	
		MICRO: ((2)) MYELINOPATHY	
		((2)) AXONOPATHY	
		SKIN	
		GROSS:	CRUST/SCAB/SCALE
			RED CRUST, RIGHT PERIOCLAR REGION
		THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:	
		MENINGES	PIRIFORM CORTEX
		PARIETAL CORTEX	TEMPORAL CORTEX
		SEPTAL NUCLEI	CAUD NUC/PUTAMEN
		AMYGDALA	HIPPOCAMPUS
		HYPOTHALAMUS	MIDBRAIN
		CEREBELLAR W.M.	ANT COMMISSURE
		INTERNAL CAPSULE	CORPUS CALLOSUM
		CEREBELLAR CTX	CEREBELLAR NUC
		OPTIC N/CHIASM	TRIGEMINAL TRACT
		DORSAL ROOT GANG	GASSERIAN GANG
		TIBIAL NERVE	PERONEAL/SURAL N
			FRONTAL CORTEX
			OCCIPITAL CORTEX
			GLOBUS PALLIDUS
			THALAMUS
			SUBSTANTIA NIGRA
			EXTERNAL CAPSULE
			FORNIX
			OLFACTORY BULB
			SPINAL NERVE RTS
			SCIATIC NERVE

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 7
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

NECROPSY PROTOCOL

PERFUSED FEMALES

The following tissues were examined at necropsy with no significant lesions observed unless specified on individual animal page:

BRAIN, NOS	SPINAL CORD, CRV	SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE	PERONEAL/SURAL N
TAIL				

The microscopic procedures used in this study are described in the methods section of the text.

Micro diagnosis grade codes:

1=MINIMAL, 2=MILD, 3=MODERATE, 4=MARKED, 5=SEVERE, P=PRESENT

Micro diagnosis distribution codes:

()=FOCAL, (())=MULTIFOCAL, NO PARENTHESES=DIFFUSE

Micro diagnosis prefix codes:

= NEOPLASM, B = BENIGN, M = MALIGNANT, @PN = PRE-NEOPLASTIC

MICRO+ indicates histologic confirmation of preceding gross diagnosis.

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 PPM FEMALE PERFUSED

ANIMAL 800 11-MAR-94

TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS

PONS

MICRO: MICROSCOPICALLY NORMAL
THERE IS CONSIDERABLE FREEZE ARTIFACT
IN MANY AREAS OF THE
BRAIN

SPINAL CORD, LUM

MICRO: MICROSCOPICALLY NORMAL
THERE IS CONSIDERABLE FREEZE ARTIFACT

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 801 11-MAR-94

TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

SPINAL CORD, CRV

GROSS: HEMORRHAGE
2X7 MM

EYE

GROSS: TRAUMATIZED
DUE TO BLEEDING
RIGHT

MICRO: EXAMINED - NO SIGNIFICANT LESIONS

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS
DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
TIBIAL NERVE	PERONEAL/SURAL N	

ANIMAL 777 11-MAR-94

TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS

MICRO: EXAMINED - NO SIGNIFICANT LESIONS

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 0 PPM FEMALE PERFUSED

ANIMAL 777 (CONTINUED)

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX
CEREBELLAR NUC	VESTIBULAR NUC	PONS
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR
SPINAL CORD, LUM	SPINAL NERVE RTS	DORSAL ROOT GANG
GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE
PERONEAL/SURAL N		

THE FOLLOWING TISSUES WERE MISSING:
FORNIX

ANIMAL 775 11-MAR-94

TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX
CEREBELLAR NUC	VESTIBULAR NUC	PONS
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR
SPINAL CORD, LUM	SPINAL NERVE RTS	DORSAL ROOT GANG
GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE
PERONEAL/SURAL N		

THE FOLLOWING TISSUES WERE MISSING:
FORNIX

ANIMAL 809 11-MAR-94

TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

EYE

GROSS: TRAUMATIZED
RIGHT, DUE TO BLEEDING

MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	SPINAL NERVE RTS

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	0 PPM	FEMALE	PERFUSED

<u>ANIMAL</u>	<u>809 (CONTINUED)</u>		
	DORSAL ROOT GANG	GASSERIAN GANG	SCIATIC NERVE
	TIBIAL NERVE	PERONEAL/SURAL N	

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	100 PPM	FEMALE	PERFUSED
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ANIMAL 797 11-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

BRAIN, NOS
GROSS: MENINGEAL HEMORRHAGE
MILD, POSTERIOR MENINGEAL FOSSA

MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	

THE FOLLOWING TISSUES WERE MISSING:
CEREBELLAR NUC VESTIBULAR NUC PONS

ANIMAL 810 11-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	

ANIMAL 807 11-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS
MICRO: EXAMINED - NO SIGNIFICANT LESIONS
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	VESTIBULAR NUC
PONS	MEDULLA OBL	OLFACTORY BULB
OPTIC N/CHIASM	TRIGEMINAL TRACT	SPINAL CORD, CRV
SPINAL CORD, THR	SPINAL CORD, LUM	

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	100 PPM	FEMALE	PERFUSED

ANIMAL	785	11-MAR-94	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			
EYE			
		GROSS:	TRAUMATIZED
		LEFT, DUE TO BLEEDING	
MICRO: EXAMINED - NO SIGNIFICANT LESIONS			
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX	
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX	
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	
AMYGDALA	HIPPOCAMPUS	THALAMUS	
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA	
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE	
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX	
VESTIBULAR NUC	PONS	MEDULLA OBL	
OLFACTORY BULB	OPTIC N/CHIASM	TRIGEMINAL TRACT	
SPINAL CORD, CRV	SPINAL CORD, THR	SPINAL CORD, LUM	
THE FOLLOWING TISSUES WERE MISSING:			
FORNIX	CEREBELLAR NUC		
ANIMAL	799	11-MAR-94	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			
GROSS: EXAMINED - NO SIGNIFICANT LESIONS			
MICRO: EXAMINED - NO SIGNIFICANT LESIONS			
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX	
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX	
CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	AMYGDALA	
HIPPOCAMPUS	THALAMUS	HYPOTHALAMUS	
MIDBRAIN	SUBSTANTIA NIGRA	CEREBELLAR W.M.	
ANT COMMISSURE	EXTERNAL CAPSULE	INTERNAL CAPSULE	
CORPUS CALLOSUM	CEREBELLAR CTX	CEREBELLAR NUC	
VESTIBULAR NUC	PONS	MEDULLA OBL	
OLFACTORY BULB	OPTIC N/CHIASM	TRIGEMINAL TRACT	
SPINAL CORD, CRV	SPINAL CORD, THR	SPINAL CORD, LUM	
THE FOLLOWING TISSUES WERE MISSING:			
SEPTAL NUCLEI	FORNIX		

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	500 PPM	FEMALE	PERFUSED
ANIMAL	788	11-MAR-94	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			
GROSS: EXAMINED - NO SIGNIFICANT LESIONS			
MICRO: EXAMINED - NO SIGNIFICANT LESIONS			
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX	
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX	
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	
AMYGDALA	HIPPOCAMPUS	THALAMUS	
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA	
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE	
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX	
CEREBELLAR NUC	VESTIBULAR NUC	PONS	
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM	
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR	
SPINAL CORD, LUM			
THE FOLLOWING TISSUES WERE MISSING:			
FORNIX			
ANIMAL	808	11-MAR-94	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			
GROSS: EXAMINED - NO SIGNIFICANT LESIONS			
SPINAL CORD, CRV			
MICRO: MICROSCOPICALLY NORMAL			
THERE IS MARKED FREEZE ARTIFACT IN THE SECTION,			
ALTHOUGH THE VENTRAL WHITE MATTER TRACTS ARE READABLE			
AND NORMAL			
SPINAL CORD, LUM			
MICRO: MICROSCOPICALLY NORMAL			
THERE IS SEVERE FREEZE ARTIFACT IN THE WHOLE SECTION			
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX	
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX	
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	
AMYGDALA	HIPPOCAMPUS	THALAMUS	
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA	
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE	
INTERNAL CAPSULE	CORPUS CALLOSUM	CEREBELLAR CTX	
CEREBELLAR NUC	VESTIBULAR NUC	PONS	
MEDULLA OBL	OLFACTORY BULB	OPTIC N/CHIASM	
TRIGEMINAL TRACT	SPINAL CORD, CRV	SPINAL CORD, THR	
SPINAL CORD, LUM			
THE FOLLOWING TISSUES WERE MISSING:			
FORNIX			
ANIMAL	762	11-MAR-94	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			
GROSS: EXAMINED - NO SIGNIFICANT LESIONS			
MICRO: EXAMINED - NO SIGNIFICANT LESIONS			
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:			
MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX	
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX	
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS	
AMYGDALA	HIPPOCAMPUS	THALAMUS	

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	500 PPM	FEMALE	PERFUSED
<u>ANIMAL</u>	<u>762 (CONTINUED)</u>		
			HYPOTHALAMUS MIDBRAIN SUBSTANTIA NIGRA CEREBELLAR W.M. ANT COMMISSURE EXTERNAL CAPSULE INTERNAL CAPSULE CORPUS CALLOSUM FORNIX CEREBELLAR CTX CEREBELLAR NUC VESTIBULAR NUC PONS MEDULLA OBL OLFACTORY BULB OPTIC N/CHIASM TRIGEMINAL TRACT SPINAL CORD, CRV SPINAL CORD, THR SPINAL CORD, LUM
<u>ANIMAL</u>	<u>771</u>	<u>11-MAR-94</u>	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			EYE
			GROSS: TRAUMATIZED
			RIGHT, DUE TO BLEEDING
			MICRO: EXAMINED - NO SIGNIFICANT LESIONS
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			MENINGES PIRIFORM CORTEX FRONTAL CORTEX
			PARIETAL CORTEX TEMPORAL CORTEX OCCIPITAL CORTEX
			SEPTAL NUCLEI CAUD NUC/PUTAMEN GLOBUS PALLIDUS
			AMYGDALA HIPPOCAMPUS THALAMUS
			HYPOTHALAMUS MIDBRAIN SUBSTANTIA NIGRA
			CEREBELLAR W.M. ANT COMMISSURE EXTERNAL CAPSULE
			INTERNAL CAPSULE CORPUS CALLOSUM FORNIX
			CEREBELLAR CTX CEREBELLAR NUC VESTIBULAR NUC
			PONS MEDULLA OBL OLFACTORY BULB
			OPTIC N/CHIASM TRIGEMINAL TRACT SPINAL CORD, CRV
			SPINAL CORD, THR SPINAL CORD, LUM
<u>ANIMAL</u>	<u>776</u>	<u>11-MAR-94</u>	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION			GROSS: EXAMINED - NO SIGNIFICANT LESIONS
			MICRO: EXAMINED - NO SIGNIFICANT LESIONS
			THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:
			MENINGES PIRIFORM CORTEX FRONTAL CORTEX
			PARIETAL CORTEX TEMPORAL CORTEX OCCIPITAL CORTEX
			CAUD NUC/PUTAMEN GLOBUS PALLIDUS AMYGDALA
			HIPPOCAMPUS THALAMUS HYPOTHALAMUS
			MIDBRAIN SUBSTANTIA NIGRA CEREBELLAR W.M.
			ANT COMMISSURE EXTERNAL CAPSULE INTERNAL CAPSULE
			CORPUS CALLOSUM CEREBELLAR CTX CEREBELLAR NUC
			VESTIBULAR NUC PONS MEDULLA OBL
			OLFACTORY BULB OPTIC N/CHIASM TRIGEMINAL TRACT
			SPINAL CORD, CRV SPINAL CORD, THR SPINAL CORD, LUM
			THE FOLLOWING TISSUES WERE MISSING:
			SEPTAL NUCLEI FORNIX

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	1000 PPM	FEMALE	PERFUSED
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ANIMAL 791 11-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS

MIDBRAIN
MICRO: ((1)) MYELINOPATHY

VESTIBULAR NUC
MICRO: ((1)) MYELINOPATHY

PONS
MICRO: ((3)) MYELINOPATHY
((3)) AXONOPATHY

MEDULLA OBL
MICRO: ((3)) MYELINOPATHY
((3)) AXONOPATHY

TRIGEMINAL TRACT
MICRO: ((1)) MYELINOPATHY

SPINAL CORD, CRV
MICRO: ((4)) MYELINOPATHY
((3)) AXONOPATHY

SPINAL CORD, THR
MICRO: ((4)) MYELINOPATHY
((3)) AXONOPATHY

SPINAL CORD, LUM
MICRO: ((2)) MYELINOPATHY

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	SUBSTANTIA NIGRA	CEREBELLAR W.M.
ANT COMMISSURE	EXTERNAL CAPSULE	INTERNAL CAPSULE
CORPUS CALLOSUM	FORNIX	CEREBELLAR CTX
CEREBELLAR NUC	OLFACTORY BULB	OPTIC N/CHIASM
SPINAL NERVE RTS	DORSAL ROOT GANG	GASSERIAN GANG
SCIATIC NERVE	TIBIAL NERVE	PERONEAL/SURAL N

ANIMAL 794 11-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS

VESTIBULAR NUC
MICRO: ((3)) MYELINOPATHY
((2)) AXONOPATHY

PONS
MICRO: ((3)) MYELINOPATHY
((2)) AXONOPATHY

MEDULLA OBL
MICRO: ((3)) MYELINOPATHY
((3)) AXONOPATHY

SPINAL CORD, CRV
MICRO: ((4)) MYELINOPATHY
((3)) AXONOPATHY

SPINAL CORD, THR
MICRO: 4 MYELINOPATHY
((3)) AXONOPATHY

SPINAL CORD, LUM
MICRO: ((2)) MYELINOPATHY

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
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See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 PPM FEMALE		PERFUSED
<u>ANIMAL</u>	<u>794 (CONTINUED)</u>	
		PARIETAL CORTEX TEMPORAL CORTEX OCCIPITAL CORTEX SEPTAL NUCLEI CAUD NUC/PUTAMEN GLOBUS PALLIDUS AMYGDALA HIPPOCAMPUS THALAMUS HYPOTHALAMUS MIDBRAIN SUBSTANTIA NIGRA CEREBELLAR W.M. ANT COMMISSURE EXTERNAL CAPSULE INTERNAL CAPSULE CORPUS CALLOSUM CEREBELLAR CTX CEREBELLAR NUC OLFACTORY BULB OPTIC N/CHIASM TRIGEMINAL TRACT SPINAL NERVE RTS DORSAL ROOT GANG GASSERIAN GANG SCIATIC NERVE TIBIAL NERVE PERONEAL/SURAL N THE FOLLOWING TISSUES WERE MISSING: FORNIX
<u>ANIMAL</u>	<u>786 11-MAR-94</u>	
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION		
		GROSS: EXAMINED - NO SIGNIFICANT LESIONS MIDBRAIN MICRO: ((1)) MYELINOPATHY AREA OF MEDIAL LEMNISCUS, AND MEDIAL LONGITUDINAL FASCICULUS VESTIBULAR NUC MICRO: ((2)) MYELINOPATHY PONS MICRO: ((3)) MYELINOPATHY ((3)) AXONOPATHY MEDULLA OBL MICRO: ((3)) MYELINOPATHY ((3)) AXONOPATHY TRIGEMINAL TRACT MICRO: ((1)) MYELINOPATHY SPINAL CORD, CRV MICRO: ((3)) MYELINOPATHY ((3)) AXONOPATHY SPINAL CORD, THR MICRO: ((3)) AXONOPATHY ((4)) MYELINOPATHY SPINAL CORD, LUM MICRO: ((3)) MYELINOPATHY ((3)) AXONOPATHY THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL: MENINGES PIRIFORM CORTEX FRONTAL CORTEX PARIETAL CORTEX TEMPORAL CORTEX OCCIPITAL CORTEX SEPTAL NUCLEI CAUD NUC/PUTAMEN GLOBUS PALLIDUS AMYGDALA HIPPOCAMPUS THALAMUS HYPOTHALAMUS SUBSTANTIA NIGRA CEREBELLAR W.M. ANT COMMISSURE EXTERNAL CAPSULE INTERNAL CAPSULE CORPUS CALLOSUM FORNIX CEREBELLAR CTX CEREBELLAR NUC OLFACTORY BULB SPINAL NERVE RTS DORSAL ROOT GANG GASSERIAN GANG SCIATIC NERVE TIBIAL NERVE PERONEAL/SURAL N THE FOLLOWING TISSUES WERE MISSING: OPTIC N/CHIASM

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 8
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP:	1000 PPM	FEMALE	PERFUSED
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ANIMAL 767 11-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

MIDBRAIN
MICRO: ((1)) MYELINOPATHY
VESTIBULAR NUC
MICRO: ((2)) MYELINOPATHY
((2)) AXONOPATHY

PONS
MICRO: ((3)) MYELINOPATHY
((3)) AXONOPATHY

MEDULLA OBL
MICRO: ((3)) MYELINOPATHY
((3)) AXONOPATHY

TRIGEMINAL TRACT
MICRO: ((1)) MYELINOPATHY

SPINAL CORD, CRV
MICRO: ((4)) MYELINOPATHY
((3)) AXONOPATHY

SPINAL CORD, THR
MICRO: ((4)) MYELINOPATHY
((3)) AXONOPATHY

SPINAL CORD, LUM
MICRO: ((2)) MYELINOPATHY
((2)) AXONOPATHY

SKIN
GROSS: SWOLLEN
PERIOcular TISSUE, BILATERAL, MILD

THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	SUBSTANTIA NIGRA	CEREBELLAR W.M.
ANT COMMISSURE	EXTERNAL CAPSULE	INTERNAL CAPSULE
CORPUS CALLOSUM	FORNIX	CEREBELLAR CTX
CEREBELLAR NUC	OLFACTORY BULB	OPTIC N/CHIASM
SPINAL NERVE RTS	DORSAL ROOT GANG	GASSERIAN GANG
SCIATIC NERVE	TIBIAL NERVE	PERONEAL/SURAL N

ANIMAL 768 11-MAR-94
TYPE OF DEATH: SCHEDULED SACRIFICE - PERFUSION

GROSS: EXAMINED - NO SIGNIFICANT LESIONS

VESTIBULAR NUC
MICRO: ((2)) MYELINOPATHY
((2)) AXONOPATHY

PONS
MICRO: ((3)) MYELINOPATHY
BOTH LESIONS IN AREA OF MEDIAL
LONGITUDINAL FASCICULUS
((2)) AXONOPATHY

MEDULLA OBL
MICRO: ((3)) MYELINOPATHY
MEDIAL LONGITUDINAL FASCICULUS
((3)) AXONOPATHY

SPINAL CORD, CRV

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

TABLE 8

VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL NECROPSY OBSERVATIONS AND/OR MICROSCOPIC DIAGNOSES

GROUP: 1000 PPM FEMALE PERFUSED

ANIMAL 768 (CONTINUED)

MICRO: ((4)) MYELINOPATHY
LESIONS ARE IN THE VENTRAL AND
LATERAL WHITE MATTER TRACTS

((3)) AXONOPATHY
SPINAL CORD, THR

MICRO: ((4)) MYELINOPATHY
((3)) AXONOPATHY
SPINAL CORD, LUM

MICRO: ((2)) MYELINOPATHY
THE FOLLOWING TISSUES WERE MICROSCOPICALLY NORMAL:

MENINGES	PIRIFORM CORTEX	FRONTAL CORTEX
PARIETAL CORTEX	TEMPORAL CORTEX	OCCIPITAL CORTEX
SEPTAL NUCLEI	CAUD NUC/PUTAMEN	GLOBUS PALLIDUS
AMYGDALA	HIPPOCAMPUS	THALAMUS
HYPOTHALAMUS	MIDBRAIN	SUBSTANTIA NIGRA
CEREBELLAR W.M.	ANT COMMISSURE	EXTERNAL CAPSULE
INTERNAL CAPSULE	CORPUS CALLOSUM	FORNIX
CEREBELLAR CTX	CEREBELLAR NUC	OLFACTORY BULB
TRIGEMINAL TRACT	SPINAL NERVE RTS	DORSAL ROOT GANG
GASSERIAN GANG	SCIATIC NERVE	TIBIAL NERVE
PERONEAL/SURAL N		

THE FOLLOWING TISSUES WERE MISSING:
OPTIC N/CHIASM

See necropsy protocol page for list of tissues examined grossly and for explanation of grades.

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

Individual Clinical Pathology Data

(11 Pages)

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TABLE 1
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS
ABBREVIATIONS

The following abbreviations appear in hematology reports when the parameter is reported.

WBC = LEUKOCYTES ($10^3/\mu\text{l}$)
RBC = ERYTHROCYTES ($10^6/\mu\text{l}$)
HGB = HEMOGLOBIN (g/dl)
HCT = HEMATOCRIT (%)
MCV = MEAN CORPUSCULAR VOLUME (μm^3)
MCH = MEAN CORPUSCULAR HEMOGLOBIN (pg)
MCHC = MEAN CORPUSCULAR HEMOGLOBIN CONCENTRATION (g/dl)
PLT = PLATELETS ($10^3/\mu\text{l}$)
SEGS = SEGMENTED NEUTROPHILS ($10^3/\mu\text{l}$)
LYMP = LYMPHOCYTES ($10^3/\mu\text{l}$)
MONO = MONOCYTES ($10^3/\mu\text{l}$)
BASO = BASOPHILS ($10^3/\mu\text{l}$)
EOS = EOSINOPHILS ($10^3/\mu\text{l}$)
BAND = BANDED NEUTROPHILS ($10^3/\mu\text{l}$)
LMON = LARGE MONOCYTES ($10^3/\mu\text{l}$)
LGL = LARGE GRANULAR LYMPHOCYTES ($10^3/\mu\text{l}$)
IGRN = IMMATURE GRANULOCYTES ($10^3/\mu\text{l}$)
NRBC = NUCLEATED RBCs (cells/100 WBCs)
RET = RETICULOCYTES (% of RBCs)
PT = PROTHROMBIN TIME (sec)
APTT = ACTIVATED PARTIAL THROMBOPLASTIN TIME (sec)
HBOD = HEINZ BODY (%)
MHGB = METHEMOGLOBIN (g/dl)
CLOT = CLOTTED
QNS = QUANTITY NOT SUFFICIENT
LA = LAB ACCIDENT
NOS = NO SAMPLE
DE = DATA ELIMINATED

CLINPATHREPORTSWINP
JANUARY 27, 1995

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL HEMATOLOGY										
MALES GROUP: 0 PPM										
DAY 10										
ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
717	7.83	15.0	43.7	56.	19.1	34.2	660.	6.2	0.52	5.49
735	7.63	15.1	42.4	56.	19.7	35.5	648.	5.0	0.33	4.60
752	7.81	15.3	43.7	56.	19.5	34.9	632.	5.1	0.41	4.55
715	7.90	15.3	44.6	56.	19.3	34.2	CLOT	7.8	1.10	6.44
711	7.76	15.1	43.4	56.	19.4	34.7	678.	5.5	0.34	5.04
750	7.58	14.8	43.1	57.	19.5	34.3	738.	7.1	0.46	6.42
751	8.15	15.7	44.9	55.	19.3	35.0	630.	8.2	1.44	6.53
706	8.00	15.4	44.3	55.	19.3	34.8	639.	5.8	0.56	5.13
738	7.83	15.0	43.4	55.	19.1	34.5	647.	6.0	0.51	5.33
728	7.76	15.3	43.4	56.	19.7	35.2	696.	4.9	0.39	4.40
MEAN	7.82	15.2	43.7	56.	19.4	34.7	663.	6.2	0.61	5.39
S.D.	0.166	0.28	0.76	0.6	0.21	0.43	35.5	1.18	0.367	0.815
N	10	10	10	10	10	10	9	10	10	10
ANIMAL	MONO	BASO	EOS	BAND	LMON	LGL	IGRN	NRBC		
717	0.03	0.07	0.04							
735	0.02	0.05	0.02							
752	0.03	0.05	0.02							
715	0.01	0.07	0.20							
711	0.03	0.10	0.03							
750	0.08	0.13	0.03							
751	0.11	0.09	0.04							
706	0.05	0.06	0.03							
738	0.05	0.05	0.04							
728	0.00	0.04	0.03							
MEAN	0.04	0.07	0.05							
S.D.	0.033	0.028	0.054							
N	10	10	10							

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL HEMATOLOGY										
MALES GROUP: 100 PPM										
DAY 10										
ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
740	7.59	14.7	42.4	56.	19.3	34.6	633.	6.3	0.44	5.75
714	7.70	15.1	43.4	56.	19.7	34.9	663.	6.3	0.47	5.73
745	7.85	15.4	43.7	56.	19.6	35.1	597.	6.7	0.74	5.63
703	7.76	15.4	43.7	56.	19.8	35.1	555.	6.7	0.58	5.99
725	8.11	15.7	44.6	55.	19.4	35.3	612.	6.2	0.56	5.53
709	7.70	15.0	43.1	56.	19.4	34.7	578.	6.8	0.64	6.00
755	7.53	15.1	42.7	57.	20.1	35.5	707.	6.3	0.38	5.81
716	7.56	15.1	42.1	56.	19.9	35.7	687.	6.0	0.50	5.40
736	7.90	15.3	44.0	56.	19.3	34.7	677.	6.0	0.56	5.27
719	7.45	14.5	41.5	56.	19.4	34.9	622.	7.2	0.58	6.49
MEAN	7.71	15.1	43.1	56.	19.6	35.0	633.	6.5	0.54	5.76
S.D.	0.199	0.36	0.95	0.5	0.27	0.37	49.7	0.38	0.103	0.347
N	10	10	10	10	10	10	10	10	10	10

ANIMAL	MONO	BASO	EOS	BAND	LMON	LGL	IGRN	NRBC
740	0.03	0.07	0.05					
714	0.03	0.06	0.03					
745	0.34	0.00	0.00	0.00	0.00	0.00	0.00	1.
703	0.02	0.08	0.04					
725	0.01	0.10	0.04					
709	0.07	0.08	0.04					
755	0.11	0.03	0.01					
716	0.05	0.05	0.04					
736	0.06	0.04	0.04					
719	0.05	0.04	0.03					
MEAN	0.08	0.05	0.03	0.00	0.00	0.00	0.00	1.
S.D.	0.097	0.029	0.015	0.000	0.000	0.000	0.000	0.0
N	10	10	10	1	1	1	1	1

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL HEMATOLOGY MALES GROUP: 500 PPM DAY 10										
ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
743	7.49	14.5	41.5	55.	19.3	34.9	608.	6.0	0.39	5.45
757	7.08	13.7	40.2	57.	19.4	34.0	688.	6.3	0.40	5.71
720	7.63	14.7	42.4	56.	19.2	34.6	578.	6.0	0.41	5.49
710	7.70	14.6	42.7	55.	18.9	34.1	622.	6.2	0.42	5.63
731	6.81	13.5	38.7	57.	19.8	34.9	710.	6.3	0.46	5.72
730	7.20	14.1	40.9	57.	19.5	34.5	CLOT	6.2	0.49	5.45
722	7.45	14.5	41.5	56.	19.4	34.9	625.	6.3	0.50	5.61
721	7.64	14.5	42.1	55.	18.9	34.4	673.	5.9	0.43	5.34
713	7.67	15.1	42.7	56.	19.6	35.2	601.	6.0	0.66	5.16
724	7.67	15.0	43.1	56.	19.5	34.7	621.	6.3	0.69	5.42
MEAN	7.43	14.4	41.6	56.	19.4	34.6	636.	6.1	0.49	5.50
S.D.	0.305	0.50	1.37	0.8	0.29	0.38	44.0	0.16	0.107	0.175
N	10	10	10	10	10	10	9	10	10	10

ANIMAL	MONO	BASO	EOS	BAND	LMON	LGL	IGRN	NRBC
743	0.02	0.08	0.05					
757	0.03	0.07	0.05					
720	0.03	0.07	0.04					
710	0.03	0.09	0.02					
731	0.01	0.08	0.04					
730	0.00	0.07	0.18					
722	0.01	0.09	0.05					
721	0.01	0.06	0.04					
713	0.18	0.00	0.00	0.00	0.00	0.00	0.00	7.
724	0.02	0.10	0.08					
MEAN	0.03	0.07	0.06	0.00	0.00	0.00	0.00	7.
S.D.	0.052	0.028	0.049	0.000	0.000	0.000	0.000	0.0
N	10	10	10	1	1	1	1	1

TABLE 2
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL HEMATOLOGY										
MALES GROUP: 1000 PPM										
DAY 10										
ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
733	7.50	14.1	41.5	55.	18.8	33.9	654.	6.0	0.35	5.59
729	7.25	13.8	40.5	56.	19.0	34.0	706.	7.3	0.68	6.46
712	7.40	13.9	41.2	56.	18.8	33.7	CLOT	7.9	0.95	6.64
727	6.90	13.0	38.3	56.	18.9	33.9	665.	7.9	0.54	7.17
739	7.05	13.4	38.7	55.	19.0	34.7	789.	7.4	0.44	6.87
744	7.57	14.0	42.4	56.	18.5	33.0	842.	7.4	0.45	6.83
737	7.46	13.7.	40.9	55.	18.4	33.5	745.	6.6	0.58	5.88
723	7.14	13.5	39.3	55.	18.9	34.4	751.	6.3	0.43	5.74
732	7.33	14.0	40.5	55.	19.1	34.5	782.	8.3	0.70	7.38
746	7.12	13.3	39.0	55.	18.7	34.1	768.	7.4	0.57	6.70
MEAN	7.27	13.7	40.2	55.	18.8	34.0	745.	7.3	0.57	6.53
S.D.	0.217	0.35	1.35	0.5	0.24	0.50	60.7	0.73	0.174	0.607
N	10	10	10	10	10	10	9	10	10	10
ANIMAL	MONO	BASO	EOS	BAND	LMON	LGL	IGRN	NRBC		
733	0.02	0.04	0.04							
729	0.01	0.09	0.04							
712	0.32	0.00	0.00	0.00	0.00	0.00	0.00	4.		
727	0.02	0.09	0.04							
739	0.01	0.09	0.02							
744	0.08	0.05	0.03							
737	0.04	0.06	0.05							
723	0.02	0.07	0.04							
732	0.07	0.10	0.06							
746	0.01	0.11	0.06							
MEAN	0.06	0.07	0.04	0.00	0.00	0.00	0.00	4.		
S.D.	0.094	0.033	0.018	0.000	0.000	0.000	0.000	0.0		
N	10	10	10	1	1	1	1	1		

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL HEMATOLOGY										
FEMALES GROUP: 0 PPM										
DAY 11										
ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
800	7.68	15.1	42.7	56.	19.6	35.2	663.	7.8	0.58	6.98
764	CLOT	CLOT	CLOT	CLOT	CLOT	CLOT	CLOT	CLOT	CLOT	CLOT
803	7.77	15.1	43.7	56.	19.5	34.7	637.	6.8	0.56	6.12
801	7.96	15.4	44.6	56.	19.3	34.4	619.	7.4	0.86	6.36
784	7.68	15.4	42.4	55.	20.1	36.4	646.	7.1	0.54	6.43
783	7.41	14.8	41.2	56.	19.9	35.8	603.	6.4	0.50	5.79
778	7.76	15.4	42.4	55.	19.9	36.4	657.	7.4	0.70	6.61
777	7.71	15.0	42.4	55.	19.4	35.3	639.	7.5	0.67	6.64
775	8.16	16.2	44.6	55.	19.9	36.3	582.	9.7	1.11	8.43
809	8.12	15.9	44.6	55.	19.6	35.7	579.	7.3	0.80	6.37
MEAN	7.81	15.4	43.2	55.	19.7	35.6	625.	7.5	0.70	6.64
S.D.	0.237	0.47	1.25	0.5	0.28	0.75	31.1	0.93	0.195	0.751
N	9	9	9	9	9	9	9	9	9	9
ANIMAL	MONO	BASO	EOS	BAND	LMON	LGL	IGRN	NRBC		
800	0.02	0.12	0.04							
764	CLOT	CLOT	CLOT							
803	0.01	0.06	0.05							
801	0.11	0.07	0.03							
784	0.04	0.06	0.04							
783	0.02	0.05	0.03							
778	0.01	0.07	0.05							
777	0.03	0.07	0.06							
775	0.07	0.10	0.04							
809	0.02	0.06	0.03							
MEAN	0.04	0.07	0.04							
S.D.	0.033	0.022	0.011							
N	9	9	9							

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL HEMATOLOGY										
FEMALES GROUP: 100 PPM										
DAY 11										
ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
797	7.73	15.1	42.7	55.	19.6	35.5	582.	5.5	0.43	4.99
810	7.49	15.1	41.5	55.	20.2	36.5	597.	7.4	1.18	5.92
793	7.75	15.1	42.7	55.	19.5	35.5	609.	6.6	0.54	5.92
789	7.46	14.9	41.5	56.	19.9	35.8	698.	7.1	0.58	6.33
780	7.36	14.8	40.5	55.	20.1	36.4	619.	6.1	0.57	5.38
779	7.38	14.7	40.9	55.	19.9	35.9	612.	7.2	0.57	6.53
807	7.66	15.1	42.1	55.	19.8	36.0	642.	7.7	0.75	6.75
785	7.24	15.1	40.9	56.	20.8	36.8	493.	7.2	0.82	6.10
772	7.47	14.7	41.5	56.	19.6	35.3	695.	5.7	0.52	5.07
799	7.58	15.0	41.5	55.	19.7	36.0	623.	6.8	0.61	6.09
MEAN	7.51	15.0	41.6	55.	19.9	36.0	617.	6.7	0.66	5.91
S.D.	0.167	0.20	0.76	0.5	0.38	0.50	58.1	0.74	0.215	0.593
N	10	10	10	10	10	10	10	10	10	10
ANIMAL	MONO	BASO	EOS	BAND	LMON	LGL	IGRN	NRBC		
797	0.02	0.05	0.03							
810	0.30	0.00	0.00	0.00	0.00	0.00	0.00	0.		
793	0.04	0.04	0.04							
789	0.05	0.07	0.04							
780	0.05	0.06	0.05							
779	0.03	0.06	0.03							
807	0.07	0.07	0.04							
785	0.02	0.07	0.20							
772	0.04	0.04	0.02							
799	0.04	0.05	0.04							
MEAN	0.07	0.05	0.05	0.00	0.00	0.00	0.00	0.		
S.D.	0.084	0.021	0.055	0.000	0.000	0.000	0.000	0.0		
N	10	10	10	1	1	1	1	1		

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL HEMATOLOGY FEMALES GROUP: 500 PPM DAY 11										
ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
770	7.37	14.5	40.2	55.	19.6	36.0	648.	8.0	0.65	7.15
805	7.27	14.5	40.5	56.	19.9	35.7	CLOT	8.7	1.16	7.25
788	7.55	14.4	41.5	55.	19.0	34.7	CLOT	8.4	0.67	7.54
806	7.09	14.3	39.3	55.	20.1	36.3	660.	7.2	0.73	6.29
808	7.31	14.2	41.2	56.	19.4	34.4	684.	7.8	0.66	6.96
762	7.51	14.2	41.5	55.	18.9	34.2	669.	7.7	0.79	6.74
781	7.52	14.9	41.2	55.	19.8	36.1	683.	7.4	0.57	6.62
771	7.45	14.3	41.2	55.	19.2	34.7	696.	7.9	0.83	6.97
774	7.50	14.8	41.8	56.	19.7	35.3	CLOT	9.5	0.93	8.37
776	7.33	14.4	40.5	55.	19.6	35.5	500.	9.8	1.24	8.28
MEAN	7.39	14.4	40.9	55.	19.5	35.3	649.	8.2	0.82	7.22
S.D.	0.144	0.23	0.75	0.5	0.40	0.75	67.5	0.88	0.224	0.678
N	10	10	10	10	10	10	7	10	10	10
ANIMAL	MONO	BASO	EOS	BAND	LMON	LGL	IGRN	NRBC		
770	0.06	0.06	0.05							
805	0.04	0.09	0.19							
788	0.01	0.10	0.08							
806	0.03	0.05	0.05							
808	0.06	0.06	0.04							
762	0.04	0.06	0.06							
781	0.04	0.05	0.07							
771	0.02	0.08	0.05							
774	0.06	0.10	0.07							
776	0.05	0.08	0.12							
MEAN	0.04	0.07	0.08							
S.D.	0.017	0.019	0.045							
N	10	10	10							

TABLE 3
VINYL PIVALATE: TEN-DAY VAPOR INHALATION STUDY IN FISCHER 344 RATS

INDIVIDUAL HEMATOLOGY FEMALES GROUP: 1000 PPM DAY 11										
ANIMAL	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	WBC	SEGS	LYMP
791	7.92	15.0	43.7	55.	18.9	34.2	628.	7.4	0.66	6.60
773	7.57	14.5	40.9	54.	19.1	35.4	557.	5.9	0.46	5.37
782	7.05	13.5	38.7	55.	19.1	34.9	622.	7.6	1.22	6.08
795	7.25	14.0	39.6	55.	19.3	35.3	647.	5.2	0.55	4.57
794	7.36	14.1	40.2	55.	19.1	35.0	757.	5.9	0.88	4.72
786	7.48	13.9	40.9	55.	18.6	34.0	748.	6.0	0.57	5.30
767	7.61	14.6	42.4	56.	19.1	34.3	690.	8.1	0.84	7.08
765	6.98	13.4	37.7	54.	19.2	35.5	668.	5.1	0.46	4.44
768	7.53	14.1	41.5	55.	18.7	33.9	726.	7.9	0.82	6.93
787	7.19	13.6	39.3	55.	18.9	34.6	730.	7.9	0.80	6.98
MEAN	7.39	14.1	40.5	55.	19.0	34.7	677.	6.7	0.73	5.81
S.D.	0.285	0.50	1.78	0.6	0.24	0.59	64.7	1.19	0.235	1.054
N	10	10	10	10	10	10	10	10	10	10

ANIMAL	MONO	BASO	EOS	BAND	LMON	LGL	IGRN	NRBC
791	0.01	0.05	0.03					
773	0.04	0.04	0.03					
782	0.08	0.00	0.23	0.00	0.00	0.00	0.00	3.
795	0.03	0.03	0.03					
794	0.24	0.00	0.06	0.00	0.00	0.00	0.00	2.
786	0.02	0.03	0.04					
767	0.06	0.07	0.04					
765	0.10	0.00	0.10	0.00	0.00	0.00	0.00	0.
768	0.05	0.07	0.03					
787	0.04	0.05	0.04					
MEAN	0.07	0.03	0.06	0.00	0.00	0.00	0.00	2.
S.D.	0.065	0.027	0.063	0.000	0.000	0.000	0.000	1.5
N	10	10	10	3	3	3	3	3

Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats
Protocol, Protocol Amendments, and Protocol Deviations
(30 Pages)



BUSHY RUN RESEARCH CENTER

6702 Mellon Road, Export, Pennsylvania 15632-8902

Telephone (412) 733-5200
Telecopier (412) 733-4804

PROTOCOL

TITLE: Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

BRRC PROJECT ID: 94U1377

SPONSORS: UCAR Emulsion Systems
Union Carbide Corporation
410 Gregson Drive
Cary, NC 27511

Shell Oil Company
One Shell Plaza
P. O. Box 4320
Houston, TX 77210

TESTING FACILITY: Bushy Run Research Center (BRRC)
Union Carbide Corporation
6702 Mellon Road
Export, PA 15632-8902

Reviewed and Approved by:

Bushy Run Research Center:

Jean Sornai Chun 2/14/94
Jean S. Chun, M.S., DABT Date
Study Director

Heather D. Burling-Flayer 2/14/94
Heather D. Burling-Flayer, Ph.D. Date
Senior Manager, Inhalation Toxicology

Linda J. Calista 2/17/94
Linda J. Calista, B.S. Date
Manager, Good Laboratory
Practices/Quality Assurance

John P. Van Miller 2/17/94
John P. Van Miller, Ph.D., DABT Date
Director

Union Carbide Corporation:

Tipson R. Tyler 3/19/94
Tipson R. Tyler, Ph.D., DABT Date
Associate Director of Applied Toxicology

Walter P. Miller 3/14/94
Walter P. Miller, Ph.D. Date
Health and Product Safety Manager

Shell Oil Company:

Marcy I. Barton 3/22/94
Marcy I. Barton, DVM, Ph.D., DABVT Date
Sponsor's Representative

UNION CARBIDE CORPORATION

OBJECTIVE

The objective of this study is to evaluate the toxic effects in rats which may result from a 10-day repeated vapor inhalation exposure to the test substance. The information will be used to establish concentrations for a subsequent 90-day inhalation study.

Design and Basis for the Study

This study will consist of 3 exposure groups and an air-exposed control group for a 10-day repeated vapor inhalation exposure to the test substance. Each group will consist of 10 rats/group/sex. Animals will be exposed for 6 hours/day, 5 consecutive days for the first week. During the second week, animals will be exposed for 6 hours/day for at least 3 consecutive days.

The portions of this study conducted by BRRC will be in compliance with the following guidelines and standards:

U.S. Environmental Protection Agency (EPA), Toxic Substances Control Act (TSCA) Good Laboratory Practice (GLP) Standards, 40 CFR Part 792.

Organisation for Economic Co-operation and Development (OECD). OECD Principles of Good Laboratory Practice, C(81)30(Final).

PERSONNEL

All personnel who participate in the conduct of the study will be documented in the raw data.

PROJECT DATES

<u>Starting Date of Acclimation</u>	February 15, 1994
<u>Proposed Starting Date of Test Substance Administration</u>	February 28, 1994
<u>Proposed Date for Completion of In-Life Phase</u>	March 12, 1994
<u>Proposed Date for Submission of Draft Final Report</u>	August 12, 1994

METHODS

Test Substance

Product Name	VYNATE® Neo-5 Monomer
Chemical Name	Vinyl pivalate
CAS Registry Number	3377-92-2
Source	Union Carbide Corporation, South Charleston, WV

Sponsor Identification Number	To be added by amendment.
BRRC Sample Number	To be added by amendment.
Description	Transparent, colorless liquid.
Purity	98.8% (Material Safety Data Sheet)
Stability	The test substance is considered to be stable for the duration of the study.
Storage Conditions	The test substance will be stored refrigerated in an appropriate storage area.
Quantity	Five gallons of the test substance were ordered for the proposed study. After the assigned study has been completed, all unused test substance will be returned to the Sponsor due to the possibility of hazardous polymerization.
Reserve Sample	A reserve sample of the test substance will not be retained at BRRC due to the possibility of hazardous polymerization.
Safety	A Material Safety Data Sheet (MSDS) supplied by the Sponsor will be reviewed by all relevant personnel before their participation in the study. This review will be documented. Normal precautions for untested substances will be used. These procedures include the use of disposable Tyvek® or plastic coats or jumpsuits, hats, booties or shoe covers, and rubber gloves while in the animal rooms. Eye protection will include the use of safety glasses at all times. Disposable Tyvek® coats or smocks and appropriate gloves will be worn during administration of the test substance. In addition, monogoggles will be used when handling the test substance.
<u>Test Animals</u>	
Species and Strain	Fischer 344 rats
Supplier	Harlan Sprague Dawley Inc., Indianapolis, IN
Rationale	The Fischer 344 rat is one strain of choice for toxicity studies.
Number and Sex	A total of 55 males and 55 females will be ordered, from which 40 males and 40 females will be selected for the study.

Age and Weight

The animals will be requested to be approximately 6 weeks of age on the scheduled animal receipt date.

**Acclimation and
Pretest Evaluations**

Shortly after their arrival at the laboratory, the animals will be transported to the room selected for the study. Once in the room, the animals will be removed from the shipping cartons and examined. All animals with evidence of disease or physical abnormalities will be discarded and the reason for rejection will be recorded. If an unusually large number of animals shows evidence of disease or physical abnormalities, the entire shipment of animals will be rejected for use in the study. Animals will be randomly selected for a pretest health screen as discussed below.

All remaining animals will be housed 2 to a cage during the pretest period and will be individually housed prior to the start of exposures and during the study.

During the acclimation period, animals will be fed the same diet that will be used during the study. Animals will be observed twice daily for mortality and once a day for any overt clinical signs of disease or abnormality. Individual detailed physical examinations will be conducted and body weight will be measured at least 2 times prior to the exposure. Animals showing abnormalities deemed by the Study Director or other appropriate personnel to render the animal unacceptable for placement on the study will be sacrificed and discarded on the day observed, and the reason for sacrifice will be recorded.

Any animal whose weight gain during the acclimation period is not considered normal for this age and strain of rat, or whose absolute body weight at the second weighing is outside $\pm 20\%$ of the population mean for each sex, will not be considered for use in the study.

**Pretest Health
Screen**

A pretest health screen will be initiated within 2 days after the receipt of the animals. The pretest health screen will be performed on 3 animals/sex selected directly from the shipping cartons with as many cartons as possible being represented and will consist of examinations for fecal parasites, necropsy, and histopathologic evaluations of selected tissues. Serology testing on 5 animals/sex for Sendai virus, rat coronavirus/sialodacryoadenitis virus, and mycoplasma pulmonis will be performed approximately

2 weeks after receipt using animals not selected for the study. Serology results will be available prior to the start of the study.

Animals not selected for the study may be held for possible random serology testing. The following organisms will be included in serologic testing conducted periodically throughout the facility:

Sendai virus (SEND)
Pneumonia virus of mice (PVM)
Rat coronavirus/Sialodacryoadenitis virus (RCV/SDA)
Kilham rat virus (KRV)
Toolan's H-1 virus (H-1)
Reovirus type 3 (REO3)
Mycoplasma pulmonis (MPUL)
Mouse polio virus (GD-7)
Lymphocytic choriomeningitis virus (LCMV)
Mouse adenovirus FL/R87 (MAD)
Minute virus of mice (MVM)
Polyoma virus (POLY)

Fecal examination for parasites will be conducted using a cellophane tape test as a prestudy screen and by zinc sulfate flotation from cecal contents obtained at necropsy.

Histopathology will consist of examination of at least the following tissues: liver, kidneys, trachea, lungs, heart, spleen, salivary glands, submandibular lymph nodes, and nasal cavities.

The purpose of this screen is to determine the suitability of the population of animals proposed for this study. Therefore, the results of this screen will be available to the Study Director before the study begins.

All rats will be examined by a veterinarian shortly after their arrival and again prior to study start. The dates of the examinations will be documented in the raw data.

Identification

Each animal will be assigned a unique identification number prior to the initiation of the study. Animals considered for assignment to the study will be

identified by cage tags and tail tattoos. Animals sacrificed for use in the pretest health screen will be identified by cage tags only until sacrifice and then toe-clipped for further identification. Records will be kept documenting the fate of all animals received for the study.

Husbandry

Conditions

All animals will be housed in an appropriate animal room at BRRRC from arrival until termination of the in-life phase of the study. Stainless steel cages with wire mesh floors will be used throughout all phases of the study. Cages will be changed and sanitized at least once every 2 weeks. DACB® (Decontaminated Animal Cage Board; Shepherd Specialty Papers, Inc.) will be changed at least 3 times each week.

Temperature and humidity will be recorded using an automatic recorder. Temperature will be maintained at 66-77°F and relative humidity will be maintained at 40-70%. The temperature and humidity will be checked by a technician at each room check and a record will be kept indicating that it was done. Appropriate corrective action will be taken whenever readings outside the specified limits are observed.

The accuracy of the temperature and humidity recording devices will be checked periodically and calibrated when necessary. The verification and calibration data will be recorded. In the event that automatic recording cannot be maintained, the temperature and humidity will be manually recorded at each room check.

An automatic timer will be set to provide fluorescent lighting for a 12-hour photoperiod (approximately 0500 to 1700 hours for the light phase). In the animal room, there will be at least 10 air changes each hour.

Diet

Ground Lab Diet™ The Richmond Standard™ Certified Rodent Diet #5002 (Purina Mills, Inc.; PMI, Inc.) will be available ad libitum except during exposures. The analyses of chemical composition and possible contaminants of each batch of diet will be performed by Purina Mills, Inc. (PMI, Inc.) and the results of the analyses will be reviewed by the Study Director.

Water

Tap water (Municipal Authority of Westmoreland County, Greensburg, PA) will be available ad libitum, except during exposures, by an automatic watering system with demand control valves mounted on each rack. Water pressure and function of the individual cage rack

systems will be checked at each room check, and a record will be kept indicating it was done. Drinking water contaminant levels will be measured at approximately 9-month intervals according to the specifications of the EPA Safe Drinking Water Act Regulations and will comply with human drinking water requirements. The results of the analyses will be reviewed by the Study Director.

Administration of Test Substance

Route and Justification	Inhalation will be the route of administration. This is considered to be a meaningful way to evaluate the toxicity of chemicals with the use pattern of the test substance.
Target Exposure Concentrations	The target exposure concentrations will be added by amendment. The control group will be exposed to filtered air only.
Exposure Chambers	<p>Four stainless steel chambers with glass doors and windows for animal observations will be used. The estimated total volume of the animals will not exceed 5% of the volume of the chambers.</p> <p>Chambers will be provided with air at a flowrate of approximately 13-14 air changes each hour to ensure an adequate oxygen content of at least 19%. The airflow rate will be monitored and recorded approximately every 30 minutes. All chambers will be maintained at a slight negative pressure.</p> <p>The temperature and relative humidity of the exposure chambers will be monitored and recorded approximately 12 times during each exposure. If possible, the temperature will be maintained at $22 \pm 2^{\circ}\text{C}$, and relative humidity will be maintained between 40 to 60%. Animal cage positions will be rotated daily to compensate for any undetected differences in the environment or test substance concentrations.</p> <p>The oxygen content of the chambers during generation of the test atmosphere will be monitored before initiation of the study.</p>
Duration of Exposure	Animals selected for the study will be exposed for 6 hours/day, 5 consecutive days for the first week and 3, 4, or 5 consecutive days for the second week. The animals will be acclimated to the exposure chambers (mock exposure) for 2 days during the week prior to initiation of exposures.

**Test Substance
Analyses**

Prior to initiation of the study and at the end of the exposure regimen, a sample of test substance will be drawn, and a compositional analysis will be performed by the Sponsor.

**Vapor
Generation**

The test substance will be metered with an appropriate laboratory pump to an evaporator to produce the vapor. The temperature of the evaporator will be determined prior to the start of the study. The vapor will be diluted to the desired concentration in the evaporator with conditioned chamber supply air.

**Analysis of Vapor
Chamber Atmosphere**

Chamber concentrations of the test substance and control chamber atmosphere will be determined by a gas chromatographic technique at least 6 times during each exposure day. Chamber probes for sampling will be placed in the breathing zone of the animals. The daily nominal (estimated) chamber concentration will also be determined.

Study Design

**Group
Assignment**

Based on the second pretest body weights, the rats will be selected for the study from the remaining population. These rats will be divided into 4 experimental groups. Each group will consist of equal numbers of male and female rats based on a weight randomization procedure.

Rats not selected for the study will remain housed in the study room until the study begins and will be used as replacements in the event that any of the selected rats dies prior to the start of the study. After the selected rats have received their first exposure, all rats not selected for the study will be used for other toxicity testing, training of BRRC staff, methods development, or possible random serology testing, or they will be humanely sacrificed and discarded. The fate of all animals not selected for use in this study will be documented in the raw data.

Following body weight measurement just prior to the first exposure, statistical evaluation of the body weights for all groups will be conducted, and statistical equivalence and homogeneity of variance will be examined. In the event that either criterion is not met, rats will be switched between groups to establish statistical equivalence and homogeneity of variance. Rats with any abnormal clinical signs will

also be replaced prior to exposure and the statistical criteria will be repeated until statistically equivalent body weights for all groups are obtained.

Organization

Group	Number of Animals		Exposure Concentrations ppm
	Male	Female	
Control	10	10	0
Low	10	10	To be added by amendment
Mid	10	10	To be added by amendment
High	10	10	To be added by amendment

Experimental Evaluations

Mortality Checks and Clinical Signs

On exposure days, the rats will be observed for mortality and overt clinical signs of toxicity just prior to exposure and shortly following the exposure. Rats will also be observed on a group basis during the 6-hour exposure. On weekends and holidays, a mortality check and overt clinical signs of toxicity will be conducted in the morning. A second mortality check will be conducted in the afternoon. During each study week, a detailed examination for clinical signs of disease or abnormality, which involve animal handling, will be performed.

Observed mortality and/or clinical signs will be recorded on the day observed. Lack of clinical signs during detailed physical examinations will also be recorded.

Sacrifice of Distressed Animals

If any animal shows signs of extreme distress or is moribund, it will be sacrificed for humane reasons before the scheduled date. The Sponsor will be notified as soon as possible if it is anticipated that the sacrifice may affect the integrity of the study.

Body Weight

During the 10-day exposure period, the body weights will be measured and recorded on Days 1, 2, 5, 8, and 9 for all animals. In addition, body weight will be measured at Day 12 and preceding sacrifice (excluding animals assigned to the neuroanatomic pathologic evaluations).

Food Consumption

Food consumption measurements will be collected for Days 1-5, 5-8, and 8-10.

**Clinical Pathology
Evaluations**

Clinical investigations (hematology) will be conducted on all surviving animals following the eighth (males) and ninth (females) exposure. The order of bleeding and analysis will be alternating (1 animal from each dose group, then repeating) in order to reduce handling and time biases. All blood samples will be obtained from methoxyflurane anesthetized animals by puncture of the retroorbital sinus. On the day of the blood collection period, food will be removed from all cages, but water will be supplied ad libitum. The following procedures will be determined:

Hematology

hematocrit
hemoglobin
erythrocyte count
mean corpuscular volume (MCV)
mean corpuscular hemoglobin (MCH)
mean corpuscular hemoglobin
concentration (MCHC)
total leukocyte count
differential leukocyte count
platelet count

**Functional
Observational
Battery (FOB)**

A battery of tests designed to detect gross alterations in nervous system function will be performed for all animals during the week prior to the exposure, and prior to the eighth or ninth exposure. All animals will be examined by trained technicians who are unaware of the animals' exposure assignment. Where possible, animals of the same sex will be evaluated by the same technician to avoid the effects of possible variation between technicians. Verification of interobserver reliability will be added to the permanent study record if animals are evaluated by more than one observer. A detailed description of the measures included in the FOB and the scoring criteria used for these measures are presented in Attachment 1.

**Anatomic
Pathology
Evaluations**

At the end of the exposure regimen, 5 animals/sex/group will be anesthetized with methoxyflurane and killed by severing the brachial vessels. Any animal showing signs of severe debility, particularly if death appears imminent, will be sacrificed early to prevent loss of tissues through autolysis. All animals on the study will receive a complete necropsy and all retained tissues will be fixed in 10% neutral buffered formalin. The order of sacrifice will be randomized in advance.

The following tissues will be collected for all animals:

gross lesions¹
lungs with mainstem bronchi²
nasopharyngeal tissues
 brain (cerebral cortex, cerebellar cortex,
 medulla/pons)
 thymic region
trachea
heart
liver
 spleen
kidneys³
adrenals
 testes
 ovaries
urinary bladder
peripheral nerve (sciatic)
 eyes
spinal cord
larynx
 bone marrow smear
 submandibular lymph nodes

Tails will be saved for identification purposes.

¹Whenever possible, a border of normal appearing tissue will also be saved when gross lesions are taken.

²Lungs will be inflated with formalin by the trachea.

³The right kidney will be sectioned crosswise and the left kidney will be sectioned longitudinally for histologic processing.

Organ Weights

The following organs from all surviving animals (excluding animals assigned to the neuroanatomic pathologic evaluations) at the sacrifice will be trimmed, blotted, and weighed:

liver
 kidneys
 adrenals
 heart
 testes (males)
 ovaries (females)
 brain (including brain stem)
 spleen
 lungs

Histopathology

The underlined tissues in the list under Anatomic Pathology Evaluations will be processed histologically and examined by light microscopy for animals in the control and high exposure groups. Animals that die or are killed during the study will be handled in a manner similar to those animals that survive to scheduled sacrifice, according to their respective exposure groups.

All tissues to be examined microscopically will be processed for paraffin embedding, sectioned at 5 microns, and stained with hematoxylin and eosin. Lesions will be graded as to severity, where possible, into 5 categories (minimal, mild, moderate, marked, or severe).

If significant lesions are observed in the high dose group, those tissues will be examined for animals in the low and mid dose groups at an additional cost to the Sponsor.

Neuroanatomic Pathology

At the end of the eighth or ninth exposure, 5 animals/sex/group will be anesthetized with sodium pentobarbital and perfused in situ by intracardiac perfusion with 10% buffered neutral formalin. After perfusion, the cranium and vertebral arches covering the brain and spinal cord will be removed, and the peripheral nerves in the hind legs will also be exposed. These tissues will then be stored, until trimmed, in the same fixative as used for the perfusions.

Tissues in the high exposure and control groups will be processed for evaluation by light microscopy, while the tissues from the low and mid dose groups will be stored in appropriate fixative for possible future microscopic examination. Any rat showing signs of severe debility, particularly if death appears imminent, will be sacrificed to prevent loss of tissues through autolysis. All animals that die during the study will be given a complete necropsy, and the tissues listed under anatomic pathology evaluations will be saved and fixed in 10% neutral buffered formalin.

The following tissues for neuroanatomic pathology will be collected from the 5 animals/sex/group that survive to the termination of exposure and all animals that are sacrificed during the study (moribund animals will be perfused as described above):

forebrain¹
center of the cerebrum¹
center of the midbrain¹
cerebellum and pons¹
medulla oblongata¹
spinal cord (cervical and lumbar)²
dorsal root ganglia³
Gasserian ganglion
dorsal and ventral root fibers³
proximal sciatic nerve (above the knee)²⁻⁴
sural (fibular) nerve (below the knee)²⁻⁴
tibial nerve (below the knee)²⁻⁴

¹Cross sections of these tissues will be evaluated.

²Cross and longitudinal sections of these tissues will be evaluated.

³Longitudinal sections of these tissues will be evaluated.

⁴Peripheral nerve may also be teased based on the results of light microscopic evaluation and/or the presence of clinical signs suggesting the presence of peripheral neuropathy.

The saved tissues in the list above for animals in the control group and the high dose group will be processed histologically and examined by light microscopy. Brains and spinal cords, along with ganglia and spinal root fibers to be examined by light microscopy, will be processed for paraffin embedding, sectioned at 5-6 microns, and stained with hematoxylin and eosin, as well as with the luxol fast blue and Bielschowsky's techniques. Additional stains may also be used at the discretion of the pathologist evaluating the tissues. From 1 hind leg, the proximal sciatic nerve from above the knee level, as well as the tibial and sural nerves from below the knee, will be embedded in glycol methacrylate, sectioned at 2 microns, and stained with hematoxylin and eosin. Peripheral nerves from the other hind leg may be teased and evaluated by light microscopy if any evidence of peripheral neuropathy is detected in the methacrylate embedded sections or if indicated by neurobehavioral studies. Peripheral nerve teasing will be performed at an additional cost to the Sponsor.

If pathologic lesions are observed in tissues from animals in the high exposure group, these target tissues will be examined for animals in the lower exposure groups at an additional cost to the Sponsor.

If evidence of neuropathologic damage is observed in the initial evaluation, affected regions will be reevaluated microscopically for animals in all exposure groups. This secondary evaluation will be performed by the pathologist without knowledge of exposure group assignments. Lesions will be graded as to severity, where possible, into 5 categories (minimal, mild, moderate, marked, and severe). Reevaluation of selected areas of the nervous system will be at an additional cost to the Sponsor.

Statistical Evaluations

The data for quantitative, continuous variables will be intercompared for the exposure and control groups by Levene's test for equality of variances, analysis of variance (ANOVA), and t-tests. If the ANOVA indicates statistical significance among experimental groups, the t-tests will be used to delineate which groups differ from the control group. If Levene's test indicates homogeneity of variances, the groups will be compared by an ANOVA for equal variances followed, when appropriate, by pooled variance t-tests. If Levene's test indicates heterogeneity of variances, the groups will be compared by an ANOVA for unequal variances followed, when appropriate, by separate variance t-tests. For nonparametric or discontinuous data, the Kruskal-Wallis test followed, when appropriate, by Mann-Whitney U-tests, will be used.

Incidence data will be compared using the appropriate statistical test, generally Fisher's Exact Test. Incidence data for select FOB endpoints with ordered severity scores will be analyzed for group differences using Gamma, Kendall's Tau-B, Stuart's Tau-C, and Somers' D measures of association.

Statistical analyses will be performed using either BMDP Statistical Software or other statistical programs, as deemed appropriate. For all statistical tests, except neuropathology frequency comparisons, the probability value of less than 0.05 (2-tailed) will be used as the critical level of significance. A probability value of less than 0.05 (1-tailed) will be used as the critical level of significance for neuropathology frequency comparisons.

ALTERATION OF PROTOCOL

Alterations to this protocol may be made as the study progresses. No changes in the protocol will be made without the specific written request or consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such change will be honored. However, it then becomes the responsibility of the Sponsor to follow such verbal change with a written verification. BRRC reserves the right to revise the protocol or deviate therefrom solely at the discretion of the Study Director if prior approval of the Sponsor cannot be obtained and the integrity of the study is considered in jeopardy. In this event, the Sponsor will be notified of the alteration as soon as possible, and documentation of the change will be the responsibility of the Study Director.

RETENTION OF RECORDS

All raw data, documentation, the protocol and any amendments, specimens, and a copy of the final report generated as a result of this study will be retained in the BRRC Archives for at least 10 years.

Following the retention period specified above, the Sponsor will be contacted and given the option of taking receipt, destroying, or arranging for other storage of the data and materials. All data and materials mentioned above will remain the sole property of the Sponsor and can be removed from BRRC at the Sponsor's discretion.

REPORTS

Draft Final Report

An unaudited draft of the final report will be submitted to the Sponsor approximately 5 months after the completion of the terminal sacrifice. This report will be a comprehensive report which will include all information necessary to provide a complete and accurate description and evaluation of the test procedures and results. It will include: a summary; appropriate text discussions of the experimental design, materials and methods, and results; and summary mean or incidence tables of in-life and pathology data. In addition, it will contain appendices with individual animal data and other pertinent information.

Final Report

The draft final report will be reviewed by the Sponsor, and comments on the report will be provided to BRRC within 8 weeks from the date of submission of the draft version. BRRC will consider these comments in preparing the final report. Assuming the Sponsor's comments are received at the specified time and no major revisions are required, BRRC will submit a final report within 12 weeks of issuance of the draft report.

The final report will be audited by the Quality Assurance Unit and contain a signed quality assurance statement. It will conform to the formatting specifications of EPA PR notice 86-3.

ANIMAL USE POLICY

It is the goal of BRRRC, through the establishment and activities of the Institutional Animal Care and Use Committee, to comply with the U.S. Animal Welfare Act and the subsequent rules promulgated by the U.S. Department of Agriculture and in effect on the date of this protocol. It has been determined that the work described herein minimizes the number of animals used, is necessary, and uses the most appropriate species and strain in order to provide meaningful results and the most useful information for comparative purposes relative to previous studies. Furthermore, this study will be conducted humanely, and to the best of our knowledge, neither unnecessarily duplicates any previous work, nor can it be accomplished using currently available, validated nonanimal models.

GOOD LABORATORY PRACTICE COMPLIANCE

BRRRC, through the administration of a quality assurance program by the Good Laboratory Practice Committee and Quality Assurance Unit, assures compliance of all phases of studies conducted by BRRRC with existing regulations and generally accepted good laboratory practices.

The study will be subjected to periodic inspections and the final report will be reviewed by the BRRRC Quality Assurance Unit.

94U1377PROTOCOLAPPENDIX

OVERVIEW OF THE FUNCTIONAL OBSERVATIONAL BATTERY (FOB)

The FOB involves the evaluation and documentation of the absence or presence (or severity if appropriate) of a predetermined set of behavioral signs for individual animals. During examination, the animals will be observed in their observation cages for signs of convulsions or tremors and evaluated for posture and palpebral closure. An animal will then be removed from the observation cage and handling reactivity will be evaluated. The animal will be placed on a clean laboratory cart covered with a thin, disposable paper board. The surface of the cart will be surrounded by clear Plexiglas® walls. The animal will be observed for signs of convulsions, tremors, excessive vocalization, piloerection, and unusual behavior. Gait, body position, breathing pattern, arousal, palpebral closure, defecation, urination, and rears will also be evaluated during this initial observation period. Approach, startle, and tail pinch responses will then be evaluated using simple equipment. The animal will then be held, and pupil size, muscle tone, lacrimation, salivation, exophthalmus, emaciation, dehydration, fur appearance, crusts, and visual placing will be evaluated. Grip strength, body temperature, body weight, air righting reflexes, and hind leg splay will be subsequently evaluated using simple equipment. The FOB requires approximately 6 minutes to perform for each animal.

Two technicians will evaluate and document neurobehavioral function of the test animals while blind to the treatment of the animals.

FOB SCORING CRITERIA**Cageside Observations**

Posture	The condition and body position of the animal will be evaluated in the observation cage. Observations will be recorded as normal/awake, normal/asleep, on side/prostrate, or on stomach/prostrate.
Convulsions	The presence or absence of convulsions and the type (tonic, clonic, or both) of convulsions will be recorded. Convulsions will be graded as either single or multiple.
Tremors	The presence or absence of tremors will be recorded. The type (coarse or fine) and location of the tremors will be recorded.
Palpebral closure	The degree of closure of the eyelids will be recorded as wide open, slightly drooping, halfway shut, or completely shut.

Open Field Observations

Handling reactivity	The reaction of the animal to being removed from the observation cage and handled will be recorded as animal limp, slight/moderate resistance, or high resistance/aggressive.
Convulsions	As described above.
Tremors	As described above.
Excessive Vocalization	The presence or absence of excessive vocalization will be recorded.
Piloerection	The presence or absence of piloerection (the animal's hair stands vertical to the skin surface) will be recorded.
Unusual behavior	Behavior which occurs out of context and/or with abnormally high frequency or behaviors not associated with the normal repertoire of the species will be recorded. This could include but is not limited to retropulsion, head bobbing, continuous nonpurposeful behavior, or prostration.
Gait	The absence of gait impairment or presence of the following types of gait impairment will be recorded. Gait impairments will be graded as either present or excessive.
Ataxia	The animal displays muscular incoordination, especially when voluntary muscle movements are attempted.

Scoring criteria:

Present - The animal walks with a noticeable sway and/or rocking and/or jerky movements when walking. Animal may fall on side occasionally.

Excessive - The animal frequently falls on its back and/or side while moving. The animal may not be able to move beyond a restricted area.

Limbs exaggerated/ splayed	<p>The hindlimbs and/or forelimbs show exaggerated placement or movements.</p> <p>Scoring criteria:</p> <p>Present - The animal displays slightly abnormal placement/movement of the limbs.</p> <p>Excessive - The limbs are moved in an extremely exaggerated motion when walking. The limbs are splayed at least 45 degrees from body.</p>
Walks on Toes	<p>The animal does not place its feet in a normal heel to toe manner when walking. The hindlimbs are drawn into the body.</p> <p>Scoring criteria:</p> <p>Present - There is a noticeable alteration in body position. The back may appear to be arched/hunched. The animal walks on its toes and the distal pads of its feet.</p> <p>Excessive - The animal walks on its toes only with a severely arched/hunched body position.</p>
Hypotonic	<p>The animal is unable to support its weight but is able to move in a straight line without lurching.</p> <p>Scoring criteria:</p> <p>Present - The animal moves slowly and drags abdomen on surface.</p> <p>Excessive - The animal's limbs are apparently weak and splayed. The animal drags its abdomen on surface and has labored locomotion.</p>
Other	<p>Any other gait abnormalities are recorded as other and described in the raw data.</p>
Body Position	<p>The animal's posture while in the observation arena will be recorded as normal, hunched, on side, or on stomach.</p>
Breathing Pattern	<p>A normal respiratory pattern is characterized by rapid and shallow breaths during movement and slower, deeper breaths when the animal is stationary. The respiratory pattern will be evaluated and recorded as either normal, mouth breathing, labored, or audible.</p>

Arousal

The level of unprovoked activity in the open field will be evaluated.

Scoring criteria:

Hyperactive/hyperalert - The animal appears excited and may dart or freeze during the observation period or may sit in one place and jump at any sound or movement.

Alternating behaviors - The animal goes through a normal repertoire of behaviors consisting of periods of sniffing, rearing, exploring, grooming, etc.

Inactive/alert - The animal generally sits in one place during the majority of the observation period but appears to be aware of its surroundings.

Inactive/not alert - The animal sits in one place during the observation period and appears to be unaware of its surroundings or is in a stupor.

Palpebral closure

As described above.

Defecation

The type or absence of excrement during the observation period will be recorded as normal, none, soft, or diarrhea.

Urination

The amount of urination during the observation period will be recorded as none, present, or excessive.

Rears

The number of times the animal lifts both front legs off the surface of the cart during the observation period will be recorded.

Manipulative Observations

Approach response

The animal's reaction to being approached by an object will be recorded as no reaction, noticeable reaction, or exaggerated reaction.

Startle response

The animal's response to acoustic stimuli will be recorded as no reaction, noticeable reaction, or exaggerated reaction.

Tail pinch response

The animal's reaction to having its tail pinched with tweezers will be recorded as no reaction, noticeable reaction, or exaggerated reaction.

Pupil size	The pupil's relative size to the normal size for the test species will be graded as normal (less than 50% of the size of the eyeball but not pinpoint), increased (greater than 50% of the size of the eyeball), or decreased (pinpoint).
Muscle tone	The relative rigidity or flaccidity of the limb and abdominal musculature will be recorded as normal, increased, or decreased.
Lacrimation	Secretion or discharge of tears causing the fur to appear wet around the eyes will be graded as none, present, or excessive.
Salivation	The presence of saliva around the mouth will be recorded as none, present, or excessive.
Exophthalmus	The absence or presence of an abnormal protrusion of the eyeball.
Emaciation	Whether the animal has an excessively lean appearance.
Dehydration	Whether the pinched skin remains in a pinched position when released.
Fur appearance	The appearance of the animal's fur will be recorded as normal, unkempt, or urine stains/wetness.
Crusts	The presence or absence of a crust around the mouth, nose, or eyes.
Visual placing	The presence or absence of forelimb extension, while being held by the observer, in anticipation of grasping a surface.
Grip strength	The animal is allowed to grasp with its forelimbs a wire mesh screen attached to a push-pull strain gauge. The animal is held by the base of the tail and pulled caudally (rapidly) parallel to the plane of the screen until its grip on the screen is broken. The animal is then allowed to grasp with its hindlimbs the leading edge of another wire mesh screen attached to a push-pull strain gauge. The animal is held by the base of the tail and pulled caudally (rapidly) parallel to and across the surface of the screen until its grip on the screen is broken. Forelimb and hindlimb measurements are performed in duplicate.
Body temperature	The animal's body temperature will be measured using an electronic thermistor inserted approximately 6 to 8 cm into the animal's rectum.

Body weight

The animal's body weight will be recorded at the time of testing.

Air righting

The ability of the animal to right itself while airborne will be recorded. The animal is held upside down, with the observer's hands under its back, approximately 30 cm above the surface of the cart. The animal is then released and the manner in which it lands is recorded either as feet/coordinated, feet/uncoordinated, back, or side.

Hind leg splay

The distance between the hindlimb digit pads after falling approximately 40 cm will be recorded. The outside digit pads of both hind paws are painted using a nontoxic paint. The animal is then held in a prone position above the cart and dropped onto a clean piece of paper. The distance between the two paint marks left upon landing is measured and recorded. The trial is performed in duplicate.



BUSHY RUN RESEARCH CENTER

6702 Mellon Road, Export, Pennsylvania 15632-8902

Telephone (412) 733-5200
Telecopier (412) 733-4804

PROTOCOL AMENDMENT 1

TITLE: Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

BRRC PROJECT ID: 94U1377

SPONSORS: UCAR Emulsion Systems
Union Carbide Corporation
410 Gregson Drive
Cary, NC 27511

Shell Oil Company
One Shell Plaza
P. O. Box 4320
Houston, TX 77210

TESTING FACILITY: Bushy Run Research Center (BRRC)
Union Carbide Corporation
6702 Mellon Road
Export, PA 15632-8902

Reviewed and Approved by:

Bushy Run Research Center:

Jean S. Chun 3/1/94
Jean S. Chun, M.S., DABT Date
Study Director

Heather D. Burleigh-Flayer 3/1/94
Heather D. Burleigh-Flayer, Ph.D. Date
Senior Manager, Inhalation Toxicology

Linda J. Calista 3/7/94
Linda J. Calista, B.S. Date
Manager, Good Laboratory
Practices/Quality Assurance

John P. Van Miller 3-7-94
John P. Van Miller, Ph.D., DABT Date
Director

Union Carbide Corporation:

Tipton R. Tyler 3/9/94
Tipton R. Tyler, Ph.D., DABT Date
Associate Director of Applied Toxicology

Walter P. Miller 3/14/94
Walter P. Miller, Ph.D. Date
Health and Product Safety Manager

Shell Oil Company:

Marcy H. Banton 3/2/94
Marcy H. Banton, DVM, Ph.D., DABVT Date
Sponsor's Representative

UNION CARBIDE CORPORATION

The protocol is amended as follows:

Item 1

Location of
Protocol Addition Page 2, Test Substance

Description of
Protocol Addition . BRRC Sample Number 57-036
 Sponsor Identification Number Lot No. JGT-3B

Rationale The BRRC Sample Number and Sponsor identification number were to be added by an amendment.

Item 2

Location of
Protocol Addition Page 7, Target Exposure Concentrations

Description of
Protocol Addition The target exposure concentrations will be 0, 100, 500 and 1000 ppm.

Rationale The target concentrations were to be added by an amendment.

Item 3

Location of
Protocol Addition Page 9, Organization

Description of
Protocol Addition

Group	Number of Animals		Exposure Concentrations (ppm)
	Male	Female	
Control	10	10	0
Low	10	10	100
Mid	10	10	500
High	10	10	1000

Rationale The target concentrations were to be added by an amendment.

Item 4

Location of
Protocol Change

Page 9, Mortality Checks and Clinical Signs

Description of
Protocol Change

Detailed examinations for clinical signs of disease or abnormality, which involve animal handling, will be performed daily.

Rationale

It was requested by the Sponsor.

Item 5

Location of
Protocol Change

Page 10, Anatomic Pathology Evaluations

Description of
Protocol Change

The following tissues will also be collected for all animals:

pituitary
thyroid - parathyroid complex
thymic region
sternum
salivary gland
pancreas
epididymis
prostate
seminal vesicles
vagina
uterus (corpus and cervix)
aorta
skin
esophagus
stomach
duodenum
jejunum
ileum
cecum
colon
rectum
mammary gland (females)
skeletal muscle (gastrocnemius)
sternum
femur (including articular surface)

Rationale

It was requested by the Sponsor.

Item 6

Location of
Protocol Change

Page 12, Histopathology

Description of
Protocol Change

The spleen, stomach, and testes will also be processed histologically and examined by light microscopy for animals in the control and high exposure groups.

Rationale

It was requested by the Sponsor.

Item 7

Location of
Protocol Change

Page 12, Neuroanatomic Pathology

Description of
Protocol Change

At the end of the eighth or ninth exposure, 5 animals/sex/group will be anesthetized with sodium pentobarbital and will be perfused in situ by intracardiac perfusion with a phosphate buffered solution of 4% para-formaldehyde followed by a phosphate buffered solution of 5% glutaraldehyde. After perfusion, the calvaria overlying the brain and the vertebral arches covering the spinal cord (down to the level of the lumbar swelling) will be removed, and the peripheral nerves in the hind legs will be exposed. The brain inside the skull (with Gasserian ganglia), the spinal column down to the level of the sacrum, and the hind legs (with the peripheral nerves) will be stored refrigerated in a phosphate buffered solution of 5% glutaraldehyde to facilitate the potential future evaluation by electron microscopy. To limit glutaraldehyde-induced tissue changes that may interfere with evaluation of the tissues by light microscopy, these tissues will be trimmed within approximately 72 hours of sacrifice. Tissues which are to be evaluated by light microscopy will then be placed in 10% neutral buffered formalin. Tissues which are to be potentially evaluated by electron microscopy will continue to be stored refrigerated in 5% glutaraldehyde. Due to the degradation of tissues following longer term storage in glutaraldehyde, tissues which were saved in this preservative will be discarded 3 months after the terminal sacrifice if they are not utilized for electron microscopic examinations.

Rationale

It was requested by the Sponsor.

BRRALPROTOCOLA1VP_2V



BUSHY RUN RESEARCH CENTER

6702 Mellon Road, Export, Pennsylvania 15632-8902

Telephone (412) 733-5200
Telecopier (412) 733-4804

PROTOCOL AMENDMENT 2

TITLE: Vinyl Pivalate: Ten-Day Vapor Inhalation Study in Fischer 344 Rats

BRRC PROJECT ID: 94U1377

SPONSORS:

UCAR Emulsion Systems
Union Carbide Corporation
410 Gregson Drive
Cary, NC 27511

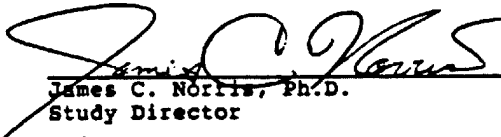
Shell Oil Company
One Shell Plaza
P. O. Box 4320
Houston, TX 77210

TESTING FACILITY:


Bushy Run Research Center (BRRC)
Union Carbide Corporation
6702 Mellon Road
Export, PA 15632-8902

Reviewed and Approved by:


Bushy Run Research Center:


James C. Norris, Ph.D.
Study Director

7/15/94
Date


Heather D. Burleigh-Flayer, Ph.D.
Senior Manager, Inhalation Toxicology

7/15/94
Date

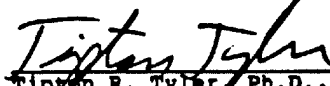

Denise L. Falt, B.S.
Representative, Quality Assurance Unit

7/21/94
Date


John P. Van Miller, Ph.D., DABT
Director

7/21/94
Date

Union Carbide Corporation:

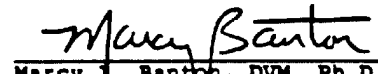

Tippen R. Tyler, Ph.D., DABT
Associate Director of Applied Toxicology

8/1/94
Date


Walter P. Miller, Ph.D.
Manager of Product Safety

8/18/94
Date

Shell Oil Company:


Marcy J. Banton, DVM, Ph.D., DABVT
Sponsor's Representative

8/25/94
Date

UNION CARBIDE CORPORATION

The protocol is amended as follows:

Item 1

Location of
Protocol Change

Page 1, Reviewed and Approved by

Description of
Protocol Change

James C. Morris, Ph.D., assumes the responsibility of
Study Director, replacing Jean S. Chun, M.S., DABT.

Rationale

Jean S. Chun is no longer employed by Bushy Run
Research Center.

Item 2

Location of
Protocol Change

Page 1, Reviewed and Approved by

Description of
Protocol Change

A representative of the Quality Assurance Unit
replaces Linda J. Calisti as signatory.

Rationale

Linda J. Calisti is no longer employed by Bushy Run
Research Center.

REHALPROTOCOLA2V2V

Protocol Deviations

All surviving animals were anesthetized with halothane instead of methoxyflurane. Methoxyflurane was not available from the supplier at the time of sacrifice.

According to the protocol, animals were to be observed once a day for overt clinical signs of disease or abnormality. Eight male and 6 female extra rats were held for an additional week without being observed for overt clinical signs.

The information from this study may be used to establish concentrations for a subsequent 90-day inhalation study; however, the study will not be conducted at BRRC.

The test substance was stored at room temperature instead of being refrigerated in an appropriate storage area.

The animals were housed in polycarbonate caging overnight prior to the functional observational battery (FOB) evaluations instead of stainless steel cages.

Modifications were made to the FOB parameters included as Attachment 1 of the protocol. The major changes were the inclusion of additional involuntary muscular movement findings and a change in the definition of ataxia. See the Appendix 7 for a listing of the parameters included in the FOB for this study and their definitions.

The animals perfused for neuroanatomic pathology evaluations were anesthetized with an i.p. injection of a mixture of sodium pentobarbital and heparin.

In addition to the oxygen content of the chambers being monitored before initiation of the study, it was also monitored during the second week of exposures.

Animals were acclimated to the exposure chambers (mock exposures) 2 weeks before the initiation of exposures, instead of 1 week in order to accommodate the pretest FOB testing performed the week prior to initiation of exposures.

A compositional analysis was not performed prior to the initiation of exposures.

In addition to the temperature of the evaporators being determined prior to the start of the study, it was also determined during the second week of exposures.

Feeders were not removed from the animals' cages prior to bleeding.

The brain was examined microscopically for all animals.

No documentation was made that the neuropathology tissues were trimmed within 72 hours following sacrifice.

It is the Study Director's belief that these protocol deviations did not affect the outcome of the study.



4

CECATE'S DATA: 0495 - 13087 SEQ. _____
Submission # 0495
TYPE: MTC 0122 21 197

CREATS DATA 0495 - 13087
SUBMISSION # 00110

IVER. NTG. 0127-21-27

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SUB DATE: 03/27/95 OUT DATE: 04/03/95 CSRAD DATE: 04/24/95

2000

Vinyl Pivalate

3

3377-98-2

INFORMATION TYPE	P.F.C.	INFORMATION TYPE	P.F.C.	INFORMATION TYPE	P.F.C.
0201 ONCO (HUMAN)	01 02 04	0204 SPECUL	01 02 04	0201 BIOLOGO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0207 HUMAN ERRORS (PROD CONTAM)	01 02 04	0202 BIOLOGO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0208 HUMAN ERRORS (ACCIDENTAL)	01 02 04	0203 CHEMISTE PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0209 HUMAN ERRORS (MISIDENTIF)	01 02 04	0204 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0210 ECONOMIA TOX	01 02 04	0205 CLASTO (ANIMAL)	01 02 04
0206 REPRODUCTO (HUMAN)	01 02 04	0211 ENV. OCCURRENCE	01 02 04	0206 CLASTO (HUMAN)	01 02 04
0207 REPRODUCTO (ANIMAL)	01 02 04	0212 HUMAN ENCS OF ENV CONTAM	01 02 04	0207 DNA DAMAGE/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0213 RESPONSE REQUEST DELAY	01 02 04	0208 PRODUCE/STROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0214 PRODUCE/STROC ID	01 02 04	0209 MISUSE	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0215 REPORTING NATIONALS	01 02 04	0210 OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0216 CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	0217 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0218 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0219 METABOLISM/ACID (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0220 METABOLISM/ACID (HUMAN)	01 02 04		

TRADE NAME	NON-CL INVENTOR	GENERAL INVENT	SERIES	TOXICOLOGICAL COMMENTS	USE	PRODUCTION
CAS SR	YES	YES (DISCONTINUED)	RAT	LOW		
	NO	NO (CONTINUES)		MED		
				HIGH		

11-11-61 Non-GP